# SYSTEMATIC ORGANIC CHEMISTRY

## MODERN METHODS OF PREPARATION AND ESTIMATION


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# PREFACE TO FIRST EDITION (1923)

THE present work is intended as a complete laboratory guide to the preparations and estimations of organic chemistry for undergraduate and post-graduate students. An endeavour has been made to introduce up-to-date methods, some of which are new, having been developed by the authors. In all cases sufficient practical details are given to enable a beginner, with the aid of the sections on apparatus and methods, to carry out the necessary operations for himself. The research student, it is hoped, will often find within the preparations required. To meet the needs of the many students whose ultimate interests are likely to be industrial, several manufacturing methods are described on a laboratory scale. An industrial experience which has been invaluable to the authors in their duties as teachers has led them to include a few notes on costing, since they feel that this subject, of such vital importance in industry, is neglected in our technical institutions.

References to the original literature have been given after almost every preparation, thus affording a means of amplifying, if desired, the practical details. Stress has been laid on the value of consulting original papers through the media of the lexicons of Richter, Beilstein and Stelzner.

Lists of suggested preparations have been included. It is believed that greater interest is developed when the student works through a sequence of preparations which are more or less intimately connected.

The authors have striven to make the book something more than a collection of recipes. Owing to deficiencies in the teaching of the subject, there is to-day a tendency for the student to think that there is a lecture-room and a laboratory variety of organic chemistry. To such an extent does this division exist that a student who in the lecture-room knows the general method for the preparation of, say, anhydrides, in the laboratory is quite at sea when asked to prepare any anhydride other than that of acetic acid. To combat this, the preparations of several compounds of a given type have been included in most sections of the book.

Many reactions of purely theoretical interest have been incorporated, so that the student may gain some real idea of the possibilities of his subject, and that he may feel his practical and theoretical text-books to be very near akin. Indeed, the authors trust that from a theoretical standpoint alone the student may find the book useful in that it will enable him to view his subject from an angle different to the usual, and in this way to gain perspective. The better to accomplish this, they have introduced a new classification of organic reactions in which reaction follows reaction on a definite plan. They hope that the student who

carefully reads through this book will not only have acquired much varied theoretical and practical knowledge, but also that his purely theoretical books will take on a new meaning, and that even their current jargon of "reducing A with HI" and "distilling B with lime" will be for him something more than a form of words.

Identifications have not been dealt with beyond including some few tests and tables of reactions. A section has been included dealing with the preparation of such inorganic compounds as are largely used in organic chemistry, and on the correct preparation of which much may depend. The authors would here emphasise the importance of introducing "oleum" of all strengths into the teaching laboratories of this country. It is of great industrial importance, cheap, and not dangerous when properly handled.

The section on estimations is rather more comprehensive than is given in most text-books of this kind, and is composed entirely of examples found to give good results in practice.

The authors beg to acknowledge assistance received directly and indirectly from well-known text-books by the following authors—Adams and others, Barnett, Barrowcliff and Carr, Cain, Cain and Thorpe, Cohen, Elbs, Fiertz-David, Fischer, Gattermann, Henderson, Knecht and Hibbert, Lassar-Cohn, Hans Meyer, Meyer-Jacobson, Meyer-Tingle, Perkin, F. M., Sudborough and James, and Ullmann.

They wish to express their thanks to Professor F. J. Wilson for his kindly interest and valuable suggestions; to Professor I. M. Heilbron for useful advice; to Mr. A. B. Crawford, B.Sc., A.R.T.C., A.I.C., and Mr. E. C. Pickering, B.Sc., A.I.C., for reading the proofs; and to Messrs. Constable & Co. for the way in which they have carried out their share of the work.

They desire to acknowledge specially the assistance rendered by Mr. James Connell, B.Sc., A.I.C., in drawing the illustrations for the book.

The authors will be grateful for any suggestions or for notification of any errors.

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# ABBREVIATIONS

| | |
|---|---|
| A. . . . | = Liebig's Annalen der Chemie. |
| Abs. A. or B. . | = British Chemical Abstracts, A or B. |
| A.C.R. . . | = Applied Chemistry Reports (S.C.I.). |
| A. Spl. . . | = Supplement Liebig's Annalen der Chemie. |
| A. Ch. . . | = Annales de Chimie et de Physique. |
| Am. Chem. . | = American Chemical Journal. |
| Am. Soc. . . | = Journal of the American Chemical Society. |
| Ann. Chim. app. | = Annali di Chimica applicata. |
| Ann. Rep. . | = Annual Reports (Chemical Society). |
| B. . . . | = Berichte der Deutschen Chemischen Gesellschaft. |
| B.P. . . | = Boiling Point. |
| Bl. . . . | = Bulletin de la Société chimique de France. |
| C. . . . | = Chemisches Zentralblatt. |
| C. & I. . . | = Chemistry and Industry. |
| C. J. R. . . | = Canadian Journal of Research. |
| C. N. . . | = Chemical News. |
| C. r. . . | = Comptes rendus de l'Académie des Sciences. |
| C. T. . . | = Chemical Trade Journal. |
| C. Z. . . | = Chemiker-Zeitung. |
| D. . . . | = Specific Gravity. |
| D.R.P. . . | = German Patent. |
| E.P. . . | = British Patent. |
| F.P. . . | = French Patent. |
| G. . . . | = Gazzetta chimica italiana. |
| H. Acta . . | = Helvetica Chimica Acta. |
| J. . . . | = Jahresbericht der Chemie. |
| J. C. S. . . | = Journal of the Chemical Society. |
| J. Eng. . . | = Journal of Industrial and Engineering Chemistry. |
| J. pr. . . | = Journal für praktische Chemie. |
| J. R. C. S. . | = Journal of the Physical and Chemical Society of Russia. |
| J. R. T. C. . | = Journal of the Royal Technical College, Glasgow. |
| J. S. C. I. . | = Journal of the Society of Chemical Industry. |
| J. Soc. Dyers . | = Journal of the Society of Dyers and Colourists. |
| M. . . . | = Monatshefte für Chemie. |
| M.P. . . | = Melting Point. |
| O. S. . . | = "Organic Syntheses" (Roger Adams, and others). |
| P. A. . . | = Poggendorf's Annalen. |
| P. C. S. . . | = Proceedings of the Chemical Society. |
| P. R. S. . . | = Proceedings of the Royal Society. |
| Phil. Mag. . | = Philosophical Magazine. |
| Phil. Trans. . | = Philosophical Transactions of the Royal Society of London. |
| Rec. . . | = Recueil des travaux chimiques des Pays-Bas. |
| T. R. S. E. . | = Transactions of the Royal Society of Edinburgh. |
| U.S.P. . . | = United States Patent. |
| Z. a. . . | = Zeitschrift für angewandte Chemie. |
| Z. Anal. . . | = Zeitschrift für analytische Chemie. |
| Z. e. . . | = Zeitschrift für Electrochemie. |
| Z. ph. . . | = Zeitschrift für physikalische Chemie. |

A table showing the dates of issue (up to 1919) of most of the above publications is given in the Introduction to "Inorganic Chemistry," by J. Newton Friend, Vol. IX., Part II.

# PREFACE TO SECOND EDITION (1931)

In responding to the call to issue a second edition we have taken the opportunity to bring the book generally up to date in all its sections.

The Apparatus and General Methods section has been increased by the addition of an outline of the mercury vapour lamp and its uses in polarimetry and in catalytic reactions. A laboratory-scale apparatus, devised by us, for the distillation of solids is included. The section on the use of the library has been extended, and attention has been drawn to the changes which have taken place in the German reference literature.

In Part II. several new reactions and preparations—or improved methods of preparation—have been introduced. Several of these are now of industrial importance. References have been brought up to date; and for those preparations described in "Organic Syntheses" references are given to this valuable series of books.

The Analytical section has been subjected to some changes. An electrically heated combustion furnace, some new methods of analysis, and the method of Rast for the determination of molecular weights, are also described. Chapter XLIV. on tests for some common organic substances has been completely rewritten.

The nomenclature used throughout the book has been amended. The principal names are those adopted by the Chemical Society. Alternative names—which are in some cases the English equivalent of the usual German names, and in others are based on the Geneva System—are given in most instances to assist the student in making reference to the original literature.

We desire to thank reviewers, teachers and students for suggestions and corrections brought to our notice. We are indebted to Professor F. J. Wilson, D.Sc., F.I.C., for his continued interest, and to Mr. H. G. A. Anderson, B.Sc., who made the additional drawings. We have also to thank Professor Thomas Gray, D.Sc., F.I.C., and Mr. Thomas Love, B.Sc., for useful suggestions.

THE ROYAL TECHNICAL COLLEGE, GLASGOW. W. M. C. AND I. V. H.

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# PREFACE TO THIRD EDITION (1937)

THE third edition appears during a transition stage in the development of organic analysis. The older macro methods are gradually giving place to micro and hemi-macro modifications. The chapters on combustion have therefore been entirely rewritten, stress being laid on the hemi-macro methods, which are perhaps more accessible to the average student. In this connection the authors have been fortunate in securing the collaboration of Dr. Robert Roger, University College, Dundee, an authority who has published widely on the subject. To him they express their deep indebtedness for his assistance in this and in other directions.

While the main plan of the book has not been altered, sections have been brought up to date by the addition of improved methods and new references, particularly to "Organic Syntheses."

With the development of large industrial research organisations there is a growing tendency to record new advances through the medium of patent literature. Frequent reference has therefore been made to this source, especially as regards high pressure reactions.

In the miscellaneous analytical section some references are given to additional exercises which the advanced student may undertake after perusal of the original literature.

The authors acknowledge with thanks suggestions made by colleagues and correspondents, and especially the services of Mr. David M. Wilson, B.Sc., who prepared the new diagrams.

The authors also thank Dr. G. D. Muir and Mr. A. C. Syme, B.Sc., A.R.T.C. for reading the proofs, and Messrs. Constable & Co. for their efficient co-operation.

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W. M. C.
I. V. H.

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# SYSTEMATIC ORGANIC CHEMISTRY

## PART I

## CHAPTER I

### INTRODUCTORY

### Cautions

1. **Fire.**—(*a*) Fire extinguishers should always be at hand in the laboratory, and should be applied *at once.*

(*b*) Great care is necessary in the use of ether, light petroleum, carbon disulphide, acetone, alcohol, benzene, etc., as the vapours of these are highly inflammable. They should always be distilled from a water bath and be collected in the apparatus shown on p. 20. Special care is necessary with carbon disulphide, as its vapour inflames in contact with a warm surface, even in the absence of a flame.

(*c*) If the liquid in a beaker or flask catches fire, the source of heat should be removed, and the flame extinguished by placing a watch-glass on the opening of the vessel.

(*d*) A blanket should be at hand in case the clothes catch fire.

2. **Poison.**—(*a*) All operations in which fumes or noxious vapours are evolved must be carried out in a good fume cupboard.

(*b*) Special care must be taken not to breathe vapours of strong or fuming acids, cyanogen, hydrogen cyanide, carbon monoxide, halogens, phosgene, alkyl sulphates, acyl chlorides, nitro compounds, aniline, etc.

(*c*) The hands should be immediately washed after using poisonous substances such as alkaloids, potassium or sodium cyanide, arsenious oxide, phosphorus. This precaution could be extended to the majority of organic compounds.

3. **Accidents.**—(*a*) A First-Aid outfit should be kept in each laboratory.

(*b*) For burns by heat, cover with a freshly prepared 20% aqueous solution of tannic acid containing 1 in 1,000 of acriflavine.

(*c*) For acid burns (1) on the skin; wash with much water and with dilute ammonia, or bicarbonate solution. (2) In the eye; use much saturated solution of borax.

(*d*) For alkalis (1) on the skin; wash with much water, then with 1% acetic acid. (2) In the eye; use much saturated boric acid solution and then drop in castor oil.

(*e*) For acid on the clothes; wash with ammonium carbonate solution.

(*f*) For alkali on the clothes; wash with dilute acetic or boric acid, and remove remaining acid with ammonium carbonate solution.

(*g*) For bromine on the skin; wash with alcohol, then with carron oil.

(*h*) For phenol burns; treat with dilute bromine water in glycerol.

All these remedies *should be kept* on a special shelf in the laboratory.

**Sodium Residues.**—These should not be dropped into the sink or waste box, but should be added in small portions to alcohol, and, when all action has ceased, the solution poured into the sink.

**Gas Masks.**—Students should acquaint themselves with gas masks for use in case of fire, explosion, or other emergency.

### Scheme of Arrangement of Reactions

The reactions in this book are grouped in sections determined by the linking of elements that occurs in the reaction to form the product. The order of the sections depends on the Richter alphabet—**C, H, O, N, Cl, Br, I, S,** etc. A complete classification by this method would take the form :—

$$\text{I. Reactions in which } \left.\begin{array}{r} \mathbf{C,} \\ \mathbf{H,} \\ \mathbf{O,} \\ \mathbf{N,} \\ \mathbf{Cl, Br, I, S,} \text{ etc.,} \end{array}\right\} \text{are linked to } \mathbf{C}.$$

$$\text{II. Reactions in which } \left.\begin{array}{r} \mathbf{H,} \\ \mathbf{O,} \\ \mathbf{N,} \\ \mathbf{Cl, Br, I, S,} \text{ etc.} \end{array}\right\} \text{are linked to } \mathbf{O}.$$

$$\text{III. Reactions in which } \left.\begin{array}{r} \mathbf{H,} \\ \mathbf{O,} \\ \mathbf{N,} \\ \mathbf{Cl, Br, I, S,} \text{ etc.} \end{array}\right\} \text{are linked to } \mathbf{N}.$$

Small sections as III. are not further subdivided in practice. Large sections are subdivided to give a separate subsection for the linking of each separate element to the main one, so to speak, of the section; and each subsection is further subdivided according to the type of compounds necessarily obtained in the various reactions. An examination of the table of contents and of the **C** to **C** section will make all the details clear. In the various sections the reactions follow one another so that related reactions come together as much as possible.

Of course, in practice, points arise which have to be settled arbitrarily. Some reactions can be placed under two or more headings, *e.g.*, $C_6H_5SH \rightarrow C_6H_5SO_3H$ might be put under **S** to **O** or **O** to **S.** In this case it is more natural to put it in the latter section, but in analogous cases the reaction in question is classified under the section first occurring. No linkings to **H** are considered, **H** is always supposed to be linked to the

other element. Some sections do not appear in the book because so few reactions fall within them.

Decomposition reactions in which links are broken rather than made, electrolytic preparations and some others are placed in a separate section.

## Hints to Students

1. Before commencing a course on practical organic chemistry, become familiar with the chapter on apparatus and methods. This chapter must be continually referred to as the course proceeds, so that facility in manipulative detail may be gained.

2. Before beginning any individual preparation read carefully the entire method and also obtain a clear idea of the theory as well as the practice of the operation. Know the reason for every step in the process.

3. Work on a definite plan, never omitting anything essential for the sake of speed.

4. Procure *suitable and sufficient* apparatus. This applies especially to the use of vessels appropriate to the quantities to be used.

5. Clean and, if necessary, dry all apparatus before use.

6. Fit up the apparatus carefully and compactly, paying particular attention to the boring and fitting of corks.

7. Follow exactly the instructions given. Definite times, temperatures and weights are not specified for nothing.

8. Cultivate a habit of observation; observe all changes and record them. This is one of the essentials of successful research.

9. Whenever possible, control the course of the reaction by testing samples. This will in many cases enable the end point to be determined exactly (see Acetanilide, Benzenesulphonic Acid).

10. Remember that the criterion of practical work is the yield of *pure* substance obtained, and if this differs by more than 10% from the yield stated, seek the cause of this difference, and then *repeat* the experiment.

11. After the experiment expand the notes already taken, giving particulars of the yield, physical characteristics (M.P., B.P., D., and microscopic examination for crystalline form) of the product. The ratio of the yield obtained to the theoretical yield also should be recorded as a percentage.

12. Cost the preparation (see p. 6) and compare the price with the current value if quoted.

13. A sample of each stable product should be kept in a specimen bottle, and details of physical characteristics and yield placed on the label.

14. Above all, keep the bench neat and clean. Use separate dusters for it and for the apparatus.

## The Use of the Library

The references given in this book to the reactions and preparations should be consulted where possible by the student.

A knowledge of the literature is of fundamental importance. Richter's Lexicon must be used where a reference for a preparation is not given. The method of using this lexicon is fully described in the preface to that book. To facilitate the use of this lexicon, molecular formulæ have been given in this book.

Richter also gives references to Beilstein which should afterwards be consulted, and the latter book always gives an indication of the scope of the reference. "A Brief Introduction to the Use of Beilstein's Handbuch der Organischen Chemie" (Huntress) has been published in English (Chapman & Hall, 1930).

The Lexicon of Stelzner should be consulted for references from 1910—1921, while the formula register of Chemisches Zentralblatt, based on the same plan as Richter and Stelzner, continues the index. Volumes 1922—1930 of this index have appeared and Volume 1930—1934 is appearing in parts. A general register is also supplied by the Chemisches Zentralblatt from 1925 onwards.

*British Chemical Abstracts* (Sections A and B) issued by the Bureau of Chemical Abstracts, and *Chemical Abstracts* of the American Chemical Society, should also be consulted for recent references.

Cultivate a habit of reading the current journals, especially J. C. S., J. S. C. I., Berichte and Am. Soc. Do not forget that organic chemistry is not the only branch of the subject. Pay particular attention to the Annual Reports issued by the Chemical Society and the Society of Chemical Industry.

## Nomenclature

The nomenclature used in this book is that according to The Chemical Society.

Alternative names are given in preparations to assist the student in looking up the literature in Richter and in Beilstein. There are also appended in some cases, in square brackets, the names according to the Geneva Commission of 1892. Although the latter has not been uniformly adopted in different countries, it is well that the student should become acquainted with this type of nomenclature, in which the name is derived, in general, from the parent hydrocarbon, and which is sometimes adopted, perhaps with slight modification, to designate a compound of complex structure.

## Suggested Lists of Preparations

Before commencing a course in practical organic chemistry, the student should have a definite list of preparations to follow. These should be arranged in increasing order of difficulty, and in such a way that, as far as possible, each preparation leads naturally to the next. Where several students are working in the laboratory, the best results are obtained when each works through a different list and compares notes with his neighbour.

The following lists are suggested :—

| | I. | II. | III. | IV. |
|---|---|---|---|---|
| 1 | No. 199 | No. 143 | No. 321 | No. 478 |
| 2 | ,, 266, 269 | ,, 321 | ,, 184 | ,, 311 |
| 3 | ,, 34, 37 | ,, 218 | ,, 195 | ,, 218 |
| 4 | ,, 409, 479 | ,, 198, 200 | ,, 160 | ,, 441 |
| 5 | ,, 75 | ,, 101 | ,, 482 | ,, 226 |
| 6 | ,, 184 | ,, 375 | ,, 337 | ,, 360 |
| 7 | ,, 249 | ,, 426 | ,, 274 | ,, 385 |
| 8 | ,, 228 | ,, 224 | ,, 230 | ,, 187 |
| 9 | ,, 361 | ,, 359 | ,, 288 | ,, 217 |
| 10 | ,, 293 | ,, 292 | ,, 364 | ,, 271 |
| 11 | ,, 384 | ,, 386 | ,, 278 | ,, 189, 265 |
| 12 | ,, 225 | ,, 284 | ,, 243 | ,, 486 |
| 13 | ,, 371 | ,, 140 | ,, 292 | ,, 376 |
| 14 | ,, 369 | ,, 241 | ,, 383 | ,, 457 |
| 15 | ,, 131 | ,, 338 | ,, 109 | ,, 289 |
| 16 | ,, 245 | ,, 29, 36 | ,, 46 | ,, 398 |
| 17 | ,, 248 | ,, 294 | ,, 25, 166 | ,, 138 |
| 18 | ,, 342 | ,, 345 | ,, 207 | ,, 272 |
| 19 | ,, 391 | ,, 278 | ,, 344 | ,, 43 |
| 20 | ,, 390 | ,, 21, 57 | ,, 157 | ,, 442 |
| 21 | ,, 20, 56 | ,, 393 | ,, 21 | ,, 51, 52 |

More advanced students should work through a synthesis involving several steps, *e.g.*, Collidine, and should also attempt the preparation of homologues of some of the substances given in detail. In the lists given above, several preparations of industrial importance are included.

These preparations should be prefaced by exercises in fractional crystallisation and fractional distillation (pp. 13, 22, 24).

Tests on groups of organic compounds, such as those outlined in Chapter XLIII, should be interspersed during the preparation exercises.

## Note on Costing

The student should always acquaint himself with the cost of the materials he uses in a preparation. He should therefore consult the price list of some well-known manufacturer or retailer. Such a list should be available in every laboratory. Having ascertained such prices, he should always, after completing his preparation, calculate the cost of his final product, and compare with the price in the price list. Many factors control the market prices, such as labour, recovery of by-products, etc. ; it is, nevertheless, a good exercise to make this comparison. In deciding which particular method of preparation should be adopted in a particular case, the student should consider the question of cost, weighing up the cost of starting materials, reagents, solvents, with yield. For example, there is a well-known reaction by which aromatic amines are converted into the corresponding hydrocarbons. It would be little short of a crime, however, except in order to confirm the reaction, to attempt to prepare toluene from toluidine in this way, since the value of the final product is only a fraction of that of the starting material, apart altogether from the cost of the reagents required ; often such reactions can well be studied in a test-tube.

Such evaluation should be adopted in all the simpler preparations. In this way the student will become acquainted with the elements of costing which play such an important part in his later life in the factory. He should hardly wait until he enters the factory to appreciate the cost of such common substances as sulphuric acid, benzene, aniline, naphthalene ; he should be able to estimate roughly the cost of derivatives such as dinitrobenzene, *p*-nitroaniline, etc. Even should he not take up the industrial side of his profession, he should be acquainted with the relative value of the more common products, and trained to decide for himself whether, for example, it would be more economical to extract with ether or benzene, taking into consideration the relative efficiencies of the two processes.

Moreover, he should not use chemically pure products for his preparations, unless for research purposes. The ordinary technical qualities supplied by the well-known manufacturers are quite suitable for most preparations, and are, of course, much cheaper. It should be remembered that the facilities for the purification of many organic products are much greater on the large scale than in the laboratory, and that these technical products are often therefore of remarkable purity. It is a valuable

exercise to purify some technical product of poor quality and again to estimate the cost of such purification (see Purification of Crude Anthracene).

The authors would not stress the point further in a book of this kind. Their experience teaches them that too often do students look upon such things as gas and power, bench reagents, and the commoner organic chemicals supplied from the departmental store, as commodities which have no actual value. It is a moot point as to whether educational authorities would not render much greater service to the student by charging more moderate fees for instruction, and thereafter charging for all materials used in the course of his work.

# CHAPTER II

## APPARATUS AND METHODS

### Practical Hints

**Softening of Corks.**—Corks should always be softened before inserting in any flask and the boring performed after softening. Several methods are available. The cork may be softened in the ordinary eccentric iron press between the two rollers. It may also be rolled on the floor underneath the foot. A convenient way is to place the cork in hot or boiling water; the cork swells somewhat and becomes quite soft so that it can be made to fit various tubes or flasks. An excellent method of reducing the size of a cork is to rotate it in a flame until the outer coating has charred; it is then rolled and cleaned: a cork thus treated may be used for vacuum distillations as the layer of carbon forms a good seal.

Corks impregnated with sodium silicate solution resist attack by hydrogen chloride and chlorine.

Rubber stoppers should be occasionally rubbed with a little toluene, which prevents hardening and keeps them clean. A trace of vaseline smeared on a rubber stopper affords considerable protection from the actions of halogens. Rubber stoppers should always be removed from vessels while the latter are still warm, to prevent sticking to the glass.

**Boring of Corks.**—Sharp borers should always be used. The end of the cork is placed against some solid object and bored half-way through from one end. The boring should then be completed from the other end. The boring of rubber stoppers may be greatly facilitated by moistening the borer with caustic soda. Mechanical borers are now available.

**Removing Fixed Stoppers.**—Hot water should be run on to the neck of the bottle and the stopper gently tapped with another glass stopper. The neck of the bottle may be inverted in hot water for a minute and afterwards gently tapped. If these methods fail, and if the contents of the bottle are not easily inflammable, the neck of the bottle may be rotated in a flame prior to tapping. Similar methods may be applied to fixed stop-cocks.

**Ground-glass Joints.**—Apparatus provided with ground-glass joints for attachment to other pieces are available for most of the common operations and should be employed for the sake of convenience and of avoiding the introduction of impurities from corks.

### Crystallisation

The solid product obtained from a chemical reaction is seldom pure, being contaminated with various impurities and by-products. For

purification, the process of crystallisation is generally employed. As the process is of such frequent occurrence, the student should early in his course acquire proficiency in it. When dealing with products obtained in plenty, the utmost care should be taken to obtain the maximum yield of pure crystallised compound, as only by doing so can the manipulative skill be acquired which is necessary to obtain a satisfactory yield of pure compound from a product obtained in meagre quantities.

**Crystallisation by Cooling.**—The ideal solvent is one in which the compound to be obtained in pure crystalline form is insoluble in the cold, but readily soluble in the hot. Further, the impurities should either be insoluble or else very soluble. In practice such a solvent is seldom obtained, but the nearest approach to it should be selected.

The solvents most commonly employed are: water, alcohol, ether, benzene, petroleum ether, acetone, glacial acetic acid; or mixtures of water and alcohol, water and acetic acid, ether and petroleum ether, benzene and petroleum ether.

The following are frequently used: chloroform, carbon disulphide, carbon tetrachloride, ethyl acetate, pyridine, hydrochloric acid, sulphuric acid, nitrobenzene, aniline, phenol, epichlorohydrin.

The following solvents are now manufactured on the large scale for industrial purposes: ethylene dichloride, di-, tri-, and tetra-chloroethylene, tetrachloroethane, dichloroethyl ether, hexahydrobenzene, cyclohexanol, tetra- and deca-hydronaphthalene (tetralin and dekalin), triacetin, ethylene glycol, butyl alcohol, diacetone alcohol, ethyl lactate, *iso*propyl ether, etc.

**Selection of Solvent.**—In order to select a suitable solvent small quantities (each about 0·1 gm.) of the finely pulverised product are placed in several test tubes and treated with a few drops of single solvents of the above class. Where the substance dissolves easily in the cold on shaking, or does not dissolve appreciably on boiling, the solvents in question may be regarded as unsuitable. Where the substance dissolves on heating or boiling, and separates out again on cooling, the solvents are suitable; that solvent should be selected which gives good crystals in the greatest abundance. At times crystallisation does not take place owing to supercooling; in such cases the side of the test tube should be rubbed with a glass rod, or the solution should be "seeded" by the addition of a small portion of the crude product, since such operations frequently induce crystallisation. If necessary, the solution should also be cooled in ice or in a freezing mixture. With substances which are sparingly soluble in the common solvents, solvents of high boiling points such as toluene, nitrobenzene, etc., should be used.

Where no single solvent is found suitable, a mixture of two miscible solvents in one of which the product is soluble and in the other insoluble may be employed with advantage. Substances which are very soluble in cold alcohol or cold acetic acid are frequently but slightly soluble in water, and many substances which are very soluble in benzene are sparingly soluble in petroleum ether. From the preliminary investigation with

single solvents it can generally be deduced which are suitable to serve as mixed solvents. The substance is dissolved in a small quantity of one solvent and heated; the second solvent is then gradually added to the hot solution until a turbidity appears; heat is again applied until complete solution takes place, and the solution is set aside to cool. Many substances separate in an amorphous or sticky form from an alcohol-water solvent. It is important that the crystals should be sufficiently well defined that their crystalline form as well as the presence of other crystals or impurities can be detected with the aid of a lens. The crystals obtained from these preliminary tests should be preserved, to serve, if needed, to "seed" the solution containing the main bulk of the substance.

**Preparation of Solution.**—If the substance is readily soluble the heating is generally carried out in a flask (conical or ordinary) on a water bath. If considerable heating is necessary, a reflux condenser should be provided to avoid loss of solvent or danger of fire. A convenient type of reflux condenser when small quantities of liquid are being dealt with is an ordinary glass filter funnel placed stem-wise in the mouth of the flask. Should the vapour catch fire, the flame should be withdrawn and the mouth of the vessel covered with a damp cloth or with a watch-glass. Wheu the solvent is neither very volatile nor easily inflammable (*i.e.*, water or acetic acid), the heating may be performed in a beaker over a flame. Small quantities of such liquids as alcohol or benzene may be heated in a similar manner by an experienced operator. Where the resulting solution does not require filtration, a conical flask should always be used (see next section). During the heating, the contents of the vessel should be frequently shaken or stirred, since crystals, especially when they melt to a heavy oil on the bottom of the vessel, render the latter liable to crack.

In preparing the solution an excessive amount of solvent should not be employed at first; successive small quantities should be added to the boiling or nearly boiling solution until the substance just completely dissolves, or until nothing but impurity remains undissolved. With substances of low melting point care should be taken that concentrated solutions from which the substance commences to separate at temperatures above its melting point are not used. When using mixed solvents, the procedure is similar to that described for the preliminary tests; if on the addition of the second liquid (*i.e.*, water or petroleum ether) resinous impurities separate, these should be filtered off before proceeding further.

**Filtration of Hot Solution** (see also **Filtration**).—This operation is usually necessary in order to remove insoluble impurities, filter fibres, etc. When the substance does not separate rapidly from the hot solution, and the liquid filters quickly, the solution may be filtered through an ordinary funnel with a short stem, fitted with a folded filter paper (Fig. 1). Both funnel and paper should previously be warmed in a steam bath. Or, the solution may be filtered with suction, using suitable types of apparatus (Figs. 27, 28). The funnel and filtering medium should be previously warmed. When the filtrate is collected in a thick glass suction flask,

the latter should be warmed beforehand by immersion in warm water. The bell-jar form of filtering apparatus (Fig. 29) is recommended, as the hot solution can be collected in a conical flask of suitable size. For "crystallisation by cooling" a rather *wide-mouthed conical flask* should be used to contain the hot filtered solution—a filter flask serves equally well for large volumes; with *vessels of this conical type* the crystals *do not creep up the sides*, as may occur when beakers or the so-called "crystallisation dishes" are used; after separation, the crystals can easily be removed with the aid of a glass rod over the end of which a short piece of rubber tube has been drawn.

If the substance crystallises rapidly from the hot solution, a hot filter should be used. Figs. 2 and 3 show steam jacketed and hot-water jacketed filters. With a volatile and easily inflammable solvent the flame should be removed from the jacket immediately before filtering, danger of fire being

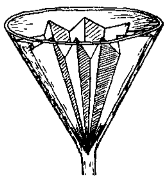


FIG. 1.

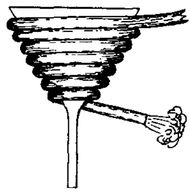


FIG. 2.

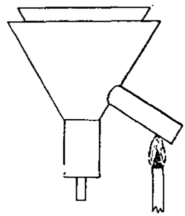


FIG. 3.

thereby avoided; in such an instance the steam funnel is preferable when the steam is generated at a safe distance.

After filtration the conical flask is covered with a watch-glass and set aside. If large crystals are required, the rate of cooling should be as slow as possible, and the flask should not be disturbed. The rate of cooling may be lessened by immersing the flask in a bath of warm water and allowing the bath and its contents to cool. If the substance separates in large coarse crystals on slow cooling, or if small pure crystals are required, it is expedient to cool quickly in cold water or in ice water, and to stir or agitate the solution at the same time. Small crystals are generally free from mother liquor, which is liable to be occluded in large crystals. When the substance is very soluble at ordinary temperature, the cooling should be continued in a freezing mixture.

The list on p. 12 gives some useful freezing mixtures, the most convenient for many purposes being a mixture of conc. hydrochloric acid and ice, or sodium chloride and ice.

**Separation of Crystals.**—This is generally effected by filtration with suction, vessels of size suitable to the quantities dealt with being selected. The crystals left on the funnel should be well pressed down and then washed a few times with small quantities of the pure solvent in order to remove the last traces of mother liquor. If the substance is easily soluble, too large quantities of solvent must not be employed for washing. When

a solvent which is not readily volatile has been used (*e.g.*, nitrobenzene, acetic acid, etc.), it must be removed from the crystals by washing with an easily volatile solvent with which it is miscible. After being thoroughly drained on the funnel, the crystals are dried (see also p. 36). They

| Mixture in gms. | Temp. falls from 15° to |
|---|---|
| 250 calcium chloride cryst. + 100 aq. | —8° |
| 8 sod. sulphate + 5 conc. HCl | —12° |
| 25 amm. chloride + 100 ice | —15° |
| 45 amm. nitrate + 100 ice | —17° |
| 50 conc. HCl + 100 ice | —18° |
| 33 sod. chloride + 100 ice | —20° |
| 1 pot. thiocyanate + 1 aq. | —24° |
| 100 dil. $H_2SO_4$ 66% + 100 ice | —31° |
| 3 calcium chloride cryst. + 2 ice | —49° |
| Solid $CO_2$ + ether | —100° |

may be placed on filter paper or porous plate, covered to protect from dust, and allowed to dry in the air, or left in a desiccator over a suitable substance to absorb the solvent; the operation may be hastened by evacuating the desiccator. If the crystals have a high melting point, the drying may be effected in a bath at temperatures below the fusion point. In this connection it should be noted that the presence of small quantities of solvent may produce a considerable lowering of the melting point. A test portion should therefore first be dried.

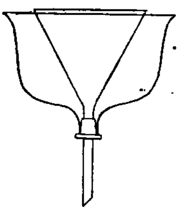


FIG. 4.

Often further crops of crystals can be obtained by concentrating the mother liquor; generally these are less pure and require to be recrystallised. In some cases the first crop has to be recrystallised before the crystals are pure (determined by M.P.). It is often convenient, in order to separate a second crop, to dilute the mother liquor with a liquid in which the dissolved substance is sparingly soluble. Crops separated in this way generally require recrystallisation.

Crystals which are very soluble in the solvent at laboratory temperature, and which have been obtained by cooling the solution in a freezing mixture, should be filtered through an ice-jacketed funnel (Fig. 4).

In all cases the process of crystallisation must be continued until no change in melting point occurs on further crystallisation, or until the product obtained by evaporating a sample of the mother liquor has the same melting point as the crystals separated from it.

On the larger laboratory scale centrifuges may be used for separating and draining crystals.

**Crystallisation by Evaporation.**—This method is employed when the substance is so easily soluble in all solvents (hot and cold) that it will only separate after partial evaporation. The solvent is allowed to evaporate spontaneously in the air or in a desiccator ; if in the latter the evaporation is greatly hastened by using a suitable absorbent as well as evacuating the desiccator. The type of vessel employed depends on the volatility of the solvent ; obviously the conical flask already recommended for " crystallisation by cooling " is not suitable for spontaneous evaporation, while a beaker or shallow " crystallising dish " is. When the latter type of vessel is used, " crusts " often form on the sides above the surface of the liquid. Such crusts seldom consist of pure substance, and they should be carefully removed with a spatula before attempting to filter off the crystals.

Since the purifying effect of crystallisation depends on the fact that the impurities remain dissolved in the mother liquor—except in cases where the impurities being insoluble are first filtered off—the solvent should never be completely evaporated, but the crystals should be filtered off while still covered with mother liquor.

*Special Methods.*—With some substances it is difficult to obtain good crystals by the methods already described. A method which frequently gives excellent results consists in dissolving the substance in some solvent, then adding a second solvent miscible with the first, but in which the substance is sparingly soluble. The first solvent is then gradually removed and the substance separates out—usually in the crystalline form. If the first solvent is the more volatile in air, spontaneous evaporation in air may diminish its concentration in the solution. The solution may be placed in a desiccator over some substance which absorbs the first solvent but not the second ; in this way water may be removed from a water-alcohol solution by solid caustic potash or quicklime.

Another method—applicable when the substance is soluble in alcohol and in ether, but insoluble in water—consists in making a saturated solution in cold alcohol, adding water until considerable precipitation has taken place, then adding ether until the precipitate has redissolved, and finally allowing the ether to diminish by spontaneous evaporation.

When a substance is soluble without change in concentrated sulphuric acid, but insoluble in water, a saturated solution in the former medium when left exposed to water-vapour—say, side by side with a vessel of water under a bell-jar—gradually absorbs water, and the substance frequently separates out in crystalline form.

The purification of many products can be facilitated by distillation, prior to crystallisation, provided they distil without decomposition. Generally it is preferable to conduct the distillation under reduced pressure (p. 26).

## Fractional Crystallisation

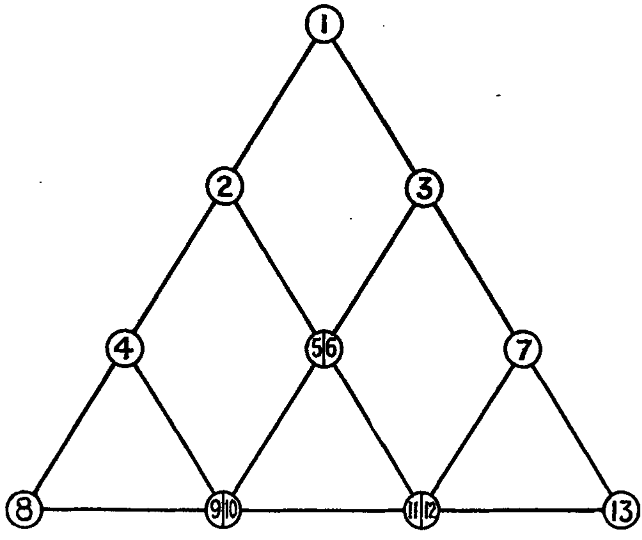
The process of fractional crystallisation is employed to separate two or more substances, all of which are soluble in the solvent used. When only two substances are present, it is often possible to find, by preliminary tests, a solvent which, when used in suitable quantity, will dissolve the whole of

the more soluble compound, but only a small quantity of the less soluble. In such a case, a preliminary separation may be effected by shaking the mixture with a quantity of solvent (hot or cold—as found suitable by trial), and filtering the solution from the residue remaining undissolved. For extracting a mixture of this nature with a hot solvent the Soxhlet apparatus (Fig. 30) is specially useful; in fact this apparatus should be employed for all extractions where a residue remains undissolved, since filtration as well as extraction is accomplished; also, only a relatively small quantity of solvent is required (see p. 34).

When commencing a fractional crystallisation, preliminary tests similar to those described under "Crystallisation" are first carried out, and the crystals which separate during such tests examined with a lens. The crystals which form first are either the least soluble or most abundant constituent of the mixture. If a second or further type of crystal appears, its shape and time of formation relative to cooling should be noted; it is often necessary to filter off the first crop while the mixture is still warm.

When dealing with a finely powdered or amorphous mixture, it is often useful to examine a small portion placed on a watch-glass under the microscope. The action of a few drops of various solvents (hot or cold) can be examined in this position, and valuable information—which might not be obvious to the naked eye—perhaps gained concerning the solubility or insolubility of some constituent in a particular solvent.

No definite plan can be given which will suit all examples of fractional crystallisation. The scheme outlined in "Text-book of Inorganic Chemistry," Vol. IV., p. 324 (J. Newton Friend), when applicable, affords a convenient method of marking and recording the various fractions involved in a fractional crystallisation; it also avoids the accumulation of a vast number of small crops and mother liquors :—



The mixture is dissolved with the aid of heat in a solvent to give solution (1). From this solution on cooling, crystals separate which are filtered off, and solution (1) is thereby divided into crop (2) and mother liquor (3). Crop (2) is dissolved in the minimum quantity of hot solvent, and from the resulting solution after cooling, crop (4) and mother liquor (5) are obtained. Mother liquor (3) is concentrated, and from the concentrated solution after cooling, crop (6) and mother liquor (7) are obtained. Crop (6) and mother liquor (5) are united to form a single fraction, and after being heated to dissolve and subsequently cooled give rise to crop (10) and mother liquor (11). Crop (4) is dissolved in a small portion of pure solvent by heating and after cooling is divided into crop (8) and mother liquor (9). Mother liquor (7) after concentration and cooling yields crop (12) and mother liquor (13). (9) and (10), likewise (11) and (12), are united to give single fractions. Proceeding in this way, the least soluble compound goes to the left in the diagram, while the most soluble goes to the right, and compounds of intermediate solubility lie between these extremes. Each crop should be tested for purity. If, when examined with the aid of a lens, two or more types of crystals are present, the crop must be recrystallised. When a crop appears uniform, a small portion should be withdrawn, dried by exposure on porous porcelain or on filter paper, and its melting point taken. In the above scheme if crop (2), say, is pure it takes no further part in the recrystallisation ; mother liquor (3) is then worked up. When the principal product is moderately soluble in the hot solvent, but not very soluble in the cold solvent, the following method might be serviceable. The product is divided into three (say) equal portions, A, B and C. A is recrystallised from the minimum quantity of pure solvent, yielding crop $A_1$. The mother liquor from $A_1$ and small quantity of washings are used to recrystallise B, yielding crop $B_1$. The mother liquor from $B_1$ is similarly used to recrystallise C. In this way the mother liquor from $C_1$ should be more or less saturated with the impurities present, while it contains but little more of the principal product than was contained in the mother liquor from $A_1$. If crop $A_1$ is impure, it is recrystallised from fresh solvent yielding crop $A_2$. Crops $B_1$ and $C_1$ are recrystallised from mother liquors $A_2$ and $B_2$, and mother liquors $C_1$ and $C_2$ are united. The process is continued after this fashion until the crop under A is pure. The crop under B then becomes the first fraction, and the mother liquors from the C's are combined and evaporated, so as to give a crop D, which becomes the new end-fraction and enters into the recrystallisations.

| | | | | |
|---|---|---|---|---|
| A | B | C | | |
| $A_1$ | $B_1$ | $C_1$ | | |
| ⋮ | ⋮ | ⋮ | | |
| An | Bn | Cn | D | |
| | ⋮ | ⋮ | ⋮ | |
| | Bm | Cm | Dm—n | E |
| | | ⋮ | ⋮ | ⋮ |

This method was found very useful for the purification of *d*-α-phenylethylamine *l*-malate (p. 408).

When the product separates from the solvent in compact crystalline masses, the mother liquor may be decanted on to the next fraction, and thus filtration, which is always attended with some slight loss of material, is avoided.

It sometimes happens that after a fractional crystallisation has been continued for some time, a solution is obtained from which two products crystallise side by side, the solution being apparently saturated with regard to each product. In such a case a separation might be effected by evaporating off the solvent and proceeding with a different solvent in which the ratio of the solubilities of the two compounds differs from the corresponding ratio in the first solvent. In some such cases mechanical means of separation might be effective; if one set of crystals is heavier than the other, the lighter set may be separated by stirring the supernatant liquor (or by rotating the vessel) and rapidly decanting. The mother liquor after filtration from the lighter crystals may be agitated a second time over the heavier crystals in order to remove any of the lighter which still remain. If one or both sets of crystals separate in fairly large form, a separation may be effected by hand picking.

## Determination of Melting Point

In order to identify a substance, or to test its purity, the melting point of the substance is determined, a process which can be rapidly carried out. If a substance does melt at all, it should, if pure, melt sharply at a definite temperature. This figure should agree with the figure given in the literature, and is valuable in the identification of a compound. If the figure is considerably lower than the one given, one must suspect impurity or else a different compound from that stated. In every case, however, the melting point should be verified by reference to Beilstein or Richter's Lexicon or Stelzner. If the melting point is higher than the figure given, the compound may be a different one, or the melting point may have been carelessly taken, for example, by heating too quickly. In general, a pure substance melts within 1° of the figure given. If the melting point is not sharp, the substance should be recrystallised from a suitable solvent before a further determination is made. From this it is obvious that great care should be observed in making this simple determination, and the following points should be carefully observed.

The choice of a thermometer is an important one. In the first place it should have a small bulb, and the range should be suitably chosen. For example, if it is known that a substance has a low melting point, a thermometer of range 0°—100° should be used. If the substance has a high melting point, a range of say 200°—300° should be chosen, and so on. All thermometers used for the determination of melting points should be standardised against a standard thermometer.

The preparation of the capillary tube requires a little practice. A piece

of thin-walled glass tubing or a test tube is heated in an ordinary Bunsen flame or blowpipe until it softens, when it is withdrawn from the flame and carefully drawn out for 2 or 3 feet. Draw slowly at first, then quicker as the glass cools and hardens. The central part, consisting of the capillary tube, is then cut into sections of about 8—10 cms. in length, and one end of each section fused in the flame. A supply of melting-point tubes should always be in readiness.

The substance of which the melting point has to be taken should be perfectly dry. A sample is ground to a fine powder on a watch-glass with a clean glass rod, introduced into the capillary tube and shaken to the

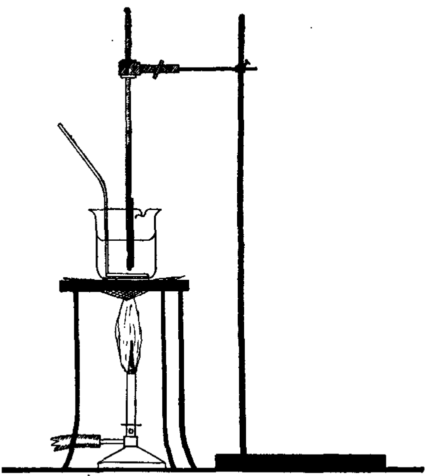


FIG. 5.

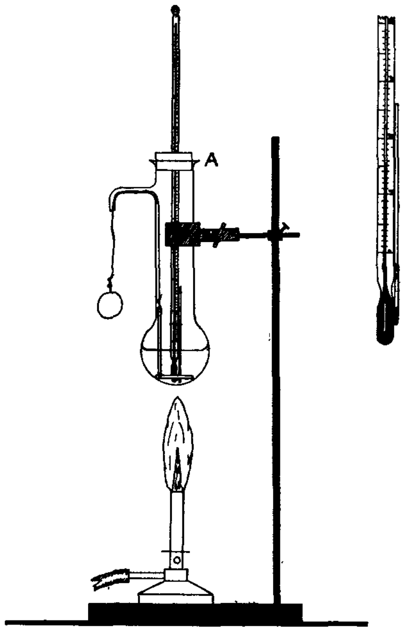



FIG. 6.

bottom ; light scratching of the tube with a file often brings this about. The tube is then ready for fixing to the thermometer. The liquid used in the melting-point apparatus is usually concentrated sulphuric acid (vaseline may also be used). After being reheated several times, sulphuric acid is apt to become discoloured. It may be rendered water-white again by adding a crystal of potassium nitrate and heating. Above 250° sulphuric acid should not be employed alone, but should be mixed with 30% or more of potassium sulphate. As this mixture is solid at ordinary temperature it should be poured out while hot. For higher temperatures fused zinc chloride or an electrically heated apparatus may be used. (J. S. C. I., 44, 577).

The melting-point apparatus consists of a small beaker or a large-sized test tube containing sulphuric acid up to a convenient level. The ther-

mometer can be held in position with its bulb well immersed in the acid by means of a clamp in the former case, or by means of a cork in the latter. It is advisable to have some kind of mechanical agitation in the sulphuric acid (see sketch) although if the heating is carefully done this may be dispensed with.

Figs. 5 and 6 show the arrangement in the two cases where a glass rod is used as a stirrer, the stirring being maintained while the acid is slowly heated. The cork at A in Fig. 6 should be as thin as possible so as to obscure the minimum amount of the scale, and if no agitator is used passing through the cork, then a slit should be made in the cork to allow exit to the vapours on heating.

The thermometer is first dipped in the sulphuric acid, and then the drop of acid which clings to the bulb is smeared on the side of the capillary tube containing the substance. The capillary tube is then made to adhere to the thermometer (Fig. 6) by capillary attraction, so that the substance in the tube is just opposite the bulb of the thermometer. This method is much better than using a rubber band, which is apt to perish in the sulphuric acid fumes, and gives rise generally to a speedy discoloration of the acid.

A cloth should be placed on the bench below the apparatus when heating is commenced, to protect the observer should an accident occur. The Bunsen burner should be held in the left hand and the stirrer worked with the right. The heating should be moderated on approaching the melting point, and the Bunsen lowered to give a flame about 2 cms. in length. The range of temperature over which the substance melts is recorded.

**Correction.**—Melting points are usually given as "uncorrected"; for correction the following formula is employed :—

$$T_c = T_o + 0{\cdot}000156l(T_o - T_m)$$

$T_c$ = corrected temperature.
$T_o$ = observed temperature.
$0{\cdot}000156$ = apparent coefficient of expansion of mercury in glass.
$l$ = length of mercury column in degrees above surface of liquid.
$T_m$ = mean temperature of mercury column, *i.e.*, the temperature of the middle point of the mercury column, taken by another thermometer.

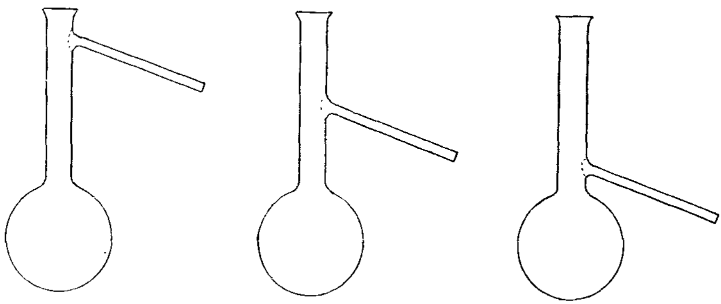
**Some Corrected Melting Points for Standardising Thermometers.**—

| | | | |
|---|---|---|---|
| *p*-Toluidine | 45° | Salicylic acid | 159·8° |
| α-Naphthylamine | 50° | Anthracene | 216° |
| Naphthalene | 80·8° | Carbazole | 246° |
| Benzoic acid | 122·5° | Anthraquinone | 285° |

"**Mixed**" **Melting Points.**—Impurities generally lower the melting point of a substance. To determine whether two substances of the same melting point are one and the same, a convenient method is to mix equal quantities of the two and take a melting point of the mixture. If the melting point is lowered the two substances are not identical.

**Setting Point.**—When a large quantity of the substance is available a very speedy determination of its setting point (freezing point) may be made as follows. The method is used largely on the technical scale, and is specially suitable for controlling chemical operations.

The substance is placed in a large test tube and melted. A thermometer reading fifths or tenths of a degree is used, and is placed in the melted substance which is stirred by means of the thermometer. The mercury in the thermometer gradually falls as the liquid cools, until it reaches a point when it jumps up suddenly (due to the heat liberated on the appearance of the solid phase). The stirring is continued, and the highest temperature to which it reaches after this upthrust is taken as the setting



(*a*) For low B.P. liquids. (*b*) For medium B.P. liquids. (*c*) For high B.P. liquids.
FIG. 7.

point or freezing point. This figure should, of course, agree with the melting point.

## Distillation and Determination of Boiling Point

The same apparatus (Fig. 8) is used for the distillation of a liquid and for determining its boiling point. A pure liquid should boil at a constant temperature, and the whole should pass over within a very small range.

The liquid to be distilled, or of which the boiling point is required, is placed in a suitable round-bottomed flask, fitted with a side tube. The flask chosen should be of suitable capacity, *e.g.*, one should not use a 500-c.c. distilling flask to distil 10 c.cs. of a liquid. The liquid should half fill the bulb of the distilling flask. Figure 7 above shows the position of the side tube for particular boiling ranges. This is important, and a proper choice will well repay the trouble taken.

**Determination of Boiling Point.**—After the liquid has been placed in the distilling flask, the thermometer which is chosen to suit the substance, as in the determination of melting points, is fixed in the neck of the flask by means of a thin cork, so that the bulb of the thermometer is opposite the exit tube.

The flask is then fixed to a Liebig or air condenser by means of a cork placed near to the neck of the flask. The condenser is attached to an

adapter at its lower end to deliver the condensed liquid into a receiver. The cork should be placed reasonably far from the end of the condenser tube. The sketch (Fig. 8) shows how the complete apparatus should

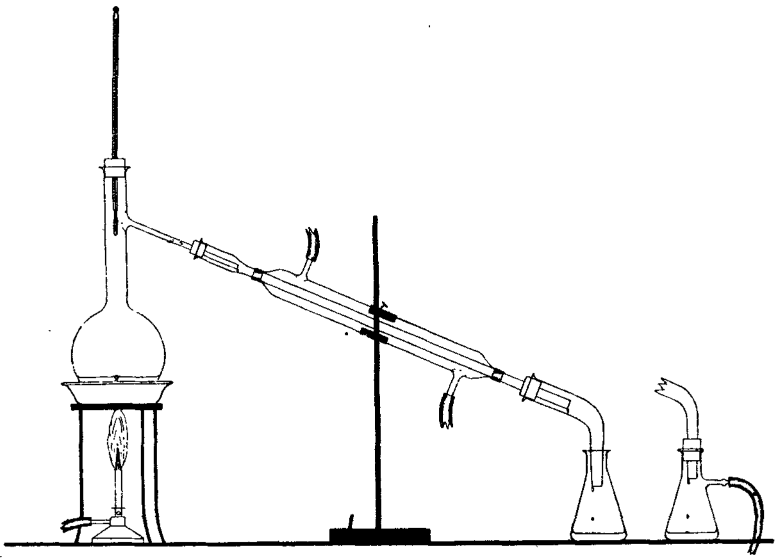


Fig. 8.

appear. The ordinary Liebig condenser should be replaced by an air condenser for liquids boiling over 160° (see Fig. 9).

When inflammable liquids are distilled, the receiver, as shown, should take the form of a Buchner flask, with a rubber tube connected to the

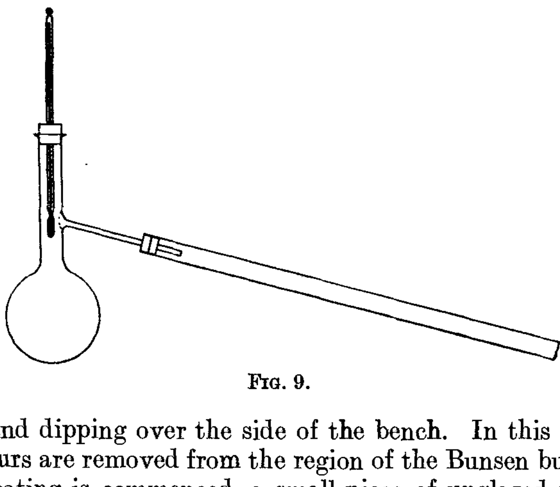


Fig. 9.

side tube, and dipping over the side of the bench. In this way inflammable vapours are removed from the region of the Bunsen burner.

Before heating is commenced, a small piece of unglazed porcelain or magnesite is introduced into the flask in order to prevent "bumping"

or too vigorous boiling. Heat is applied very gradually, and the temperature raised very slowly at first, until it reaches a point at which the liquid distils regularly. This temperature, which is the boiling point of the liquid, remains constant.

When there is only a very small quantity of liquid available, two methods may be applied :—

1. A very small distilling flask, preferably pear-shaped, may be used. The sketch (Fig. 10) shows a very useful type of flask for this purpose. These flasks can be obtained of capacity down to 1 c.c. The hood prevents condensed liquid returning to the bulb.

2. This method may be employed for even one drop of liquid. The latter is placed in a narrow tube which has been sealed at one end, and this tube is attached to a thermometer by means of a rubber band in such a position that the liquid is opposite the bulb of the thermometer. Into the liquid is now placed the open end of a sealed melting-point tube ; the whole is fixed in the melting-point apparatus. The sketch (Fig. 11) shows the arrangement.

At first bubbles of air are expelled from the end of the capillary tube due to expansion as soon as heat is applied to the acid ; the heating should be very carefully carried out. Ultimately a point will be reached at which there is a regular stream of bubbles emitted from the tube. This temperature is the boiling point. At least two observations should be made by this method, a new capillary tube being used each time. The mean is taken as the true boiling point. These boiling points are " uncorrected "—the " corrected " figure is obtained as with melting points.

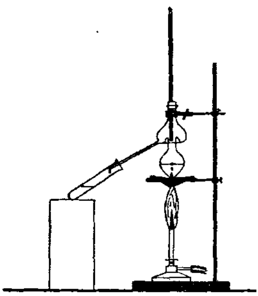


FIG. 10.

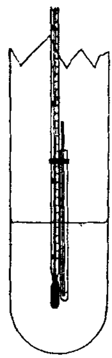


FIG. 11.

**Corrections.**—(*a*) *Thermometer Reading.*

$$T_c = T_o + 0{\cdot}000156l(T_o - T_m)$$

$T_o$ = observed boiling point.
$T_c$ = corrected boiling point.
$l$ = length of mercury column not heated by the vapours.
$T_m$ = mean temperature of mercury column (see Melting Point).

(*b*) *Barometric Pressure.*

$$T_c = T_o + 0{\cdot}043\,(760 - P)$$

P = atmospheric pressure in millimetres.

**Some Corrected Boiling Points for Standardising Thermometers.**—

| | | | |
|---|---|---|---|
| Chloroform . . . | 61·3° | Nitrobenzene . . | 210·9° |
| Benzene . . . | 80·2° | Quinoline . . . | 237·5° |
| Chlorobenzene . . | 131·2° | Benzophenone . . | 305·9° |
| Aniline . . . | 184·4° | Mercury . . . | 356·8° |

## Fractional Distillation

Fractional distillation, using the ordinary distillation apparatus, is employed for separating substances whose boiling points differ by at least 40°. The mixture is distilled slowly and the distillates are collected in separate receivers. For example, a mixture of benzene (B.P. 80·2°) and nitrobenzene (B.P. 210·9°) can be separated by collecting the distillate which comes over at about 80° in one receiver and at about 210° in another receiver. By careful redistillation of these two fractions the two receivers will ultimately contain pure benzene and pure nitrobenzene respectively.

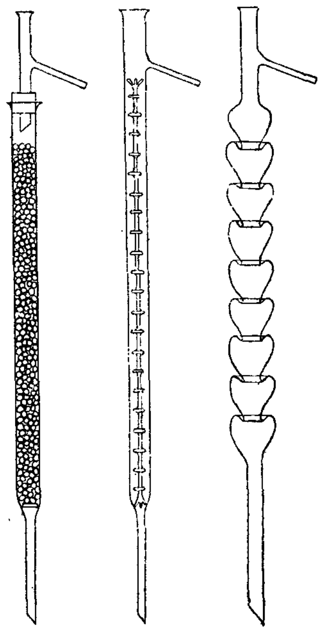


FIG. 12.

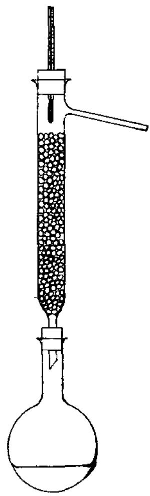


FIG. 13.

It is always necessary to repeat the process when the boiling points of the liquids are fairly close.

When the boiling points lie near one another the same method can be used, but before a separation can be obtained the process may have to be repeated ten or twenty times, and even then the separation will probably not be complete. By using still-heads or fractionating columns this difficulty can be obviated. Fig. 12 indicates the types of still-heads most commonly used in the laboratory for this purpose. The principle of all is similar; they offer a large cooling surface to the rising vapours which are always in contact with the falling condensed liquid. In this way only the more volatile liquid passes over to the condenser. Fig. 13 shows a column attached to a flask. Such an apparatus could be used for separating, say, a mixture of benzene (B.P. 80·2°) and toluene (B.P. 110°). It is

always necessary to repeat the process at least once until the constituents of the mixture give definite boiling points.

In some cases, liquids with different boiling points cannot be separated in this way, owing to the formation of constant boiling mixtures. Such mixtures cannot, therefore, be separated by distillation. The excess of each constituent beyond the constant boiling proportion would, of course, pass over, until the composition reached that of the constant boiling mixture, which has either a maximum or minimum boiling point compared with any other mixture of the substances.

The tables given below, which are taken from "A Laboratory Course of Organic Chemistry" (A. W. Titherley), show the boiling point and composition of some such constant boiling mixtures, consisting of two substances, A and B.

**Constant Boiling Mixtures**

*Minimum B.P. Type I.*

| A. | B.P. | B. | B.P. | B.P. of constant mixture. | % of A. in constant mixture. |
|---|---|---|---|---|---|
| Methyl alcohol | 65·5° | Acetone | 56·6° | 55·95° | 13·5 |
| Water | 100° | Ethyl alcohol | 78·3° | 78·15° | 4·43 |
| Water | 100° | Isopropyl alcohol | 82·45° | 80·35° | 12·10 |
| Water | 100° | *n*-Propyl alcohol | 97·2° | 87·7° | 28·31 |
| Water | 100° | Butyric acid | 159·5° | 99·2° | 80 |
| Benzene | 80·2° | Ethyl alcohol | 78·3° | 68·25° | 67·64 |
| Benzene | 80·2° | Methyl alcohol | 65·5° | 58·35° | 60·45 |
| Pyridine | 115° | Water | 100° | 92·5° | 59 |

*Maximum B.P. Type II.*

| A. | B.P. | B. | B.P. | B.P. of constant mixture. | % of A. in constant mixture. |
|---|---|---|---|---|---|
| Water | 100° | Formic acid | 99·9° | 107·1° | 23 |
| Water | 100° | HCl | about —80° | 110° | 79·76 |
| Water | 100° | HBr | ,, —73° | 126° | 52·5 |
| Water | 100° | HI | ,, —35° | 127° | 43 |
| Water | 100° | $HNO_3$ | 86° | 120·5° | 32 |
| Chloroform | 61·2° | Acetone | 56·6° | 64·7° | 80 |

The boiling points are given for 760 mms. pressure. In Type I. the boiling point of the constant boiling mixture is below that of either constituent, while in Type II. the boiling point of the constant boiling mixture is above that of either constituent.

**References.**—For theoretical considerations of this subject the student is referred to :—

Reilly, "Distillation." Robinson, "Elements of Fractional Distillation." Young, "Stoichiometry."

A very simple and ingenious type of still-head is that patented by Dufton (see J. S. C. I., 38, 45).

**Purification and Fractionation of 90% Benzol.**—Commercial benzene is far from pure and contains homologues (chiefly toluene) and thiophen as well as basic substances. On removal of the bases with dilute acid and the thiophen with conc. sulphuric acid, fairly pure benzene may be obtained by fractional distillation of the residue. "90% benzol" contains about 80—82% benzene, 14—15% toluene, and about 3% xylenes. The term means that 90% by volume of the benzol can be distilled off up to 100°.

Shake up 200 c.cs. of 90% benzol in a large separating funnel with 10 c.cs. of conc. sulphuric acid, allow to settle, and run off the acid layer. Repeat with 10 c.cs. of fresh acid. Wash the residue first with water, then with dilute caustic soda, and finally with water. Dry by standing for 12 hours over granular calcium chloride. Decant into a round-bottom flask and add a small piece of unglazed porcelain (to prevent bumping). Attach a fractionating column (Fig. 12) with thermometer and condenser. Place the apparatus in a fume cupboard or other place free from draughts. Clean, dry, and label a number of small flasks to serve as receivers.

Heat the liquid to boiling, using a very small flame and adjusting it so that a drop of distillate is obtained per second. Collect the fraction boiling up to 80° in the first receiving flask, from 80°—85° in the second, 85°—90° in the third, and so on up to 100°, then finally a fraction from 110°—115°. Remove the flame when the temperature exceeds 115° and discard the residue in flask. To the empty distilling flask add the first fraction and redistil, rejecting distillate below 79°, but collecting what distils at 79°—82°. When the temperature reaches 82° add second fraction to distilling flask, and again collect in the same receiver the distillate from 79°—82°. Similarly add fractions 3 and 4 in turn, collecting the distillate at 79°—82° in the same receiver. Redistil the fraction 79°—82°, collecting the distillate between 80°—81°, which consists almost entirely of benzene. Place this fraction in a flask surrounded by ice. When it has almost completely solidified pour off the still liquid portion, the remaining crystals being practically pure benzene.

The residue in the distilling flask after removing the fraction 79°—82° may be distilled up to 100°, and the earlier fraction boiling at 100°—115° then added. Fractions may be collected as before and the final fraction redistilled, the portion distilling at 109·5°—110·5° being collected. This consists of toluene.

## Steam Distillation

Steam distillation is sometimes employed for separating substances of high boiling point which have an appreciable vapour pressure at 100°. It consists in passing a current of steam through the mixture. The sketch (Fig. 14) shows the apparatus usually employed. The steam is generated in a tin canister or a glass flask which is provided with a long glass safety tube dipping below the surface of the water. The distilling flask should be large, and should be sloped to prevent the liquid splashing up into the condenser. The steam delivery tube should be slightly bent, as

shown. Rubber stoppers should not be used. In order to prevent excessive condensation of steam the distilling flask should be directly heated, and a soluble salt may be added to raise the temperature. The

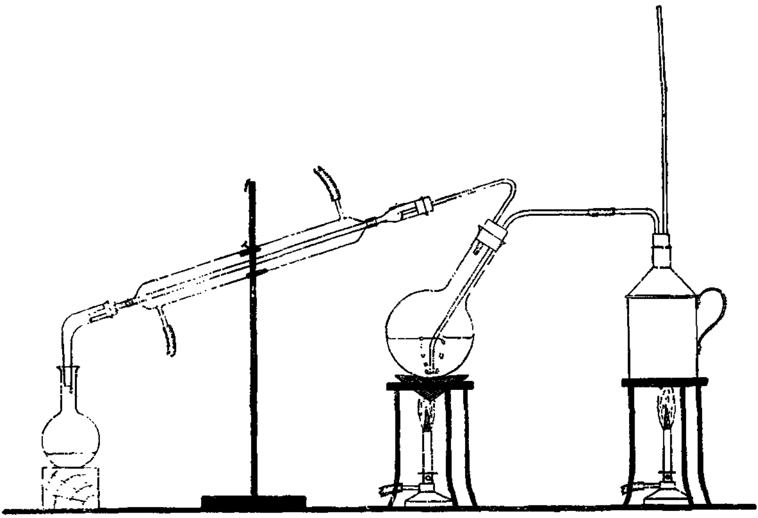


FIG. 14.

distillate may consist of a solution in water (acetic acid—see p. 473), or of two layers (aniline—see p. 356), or a solid may separate (*o*-nitrophenol—see p. 276). If the last tends to choke the condenser the cooling water should be turned off occasionally. Steam may be substituted by alcohol or ether vapour in particular cases. Control tests should be made occasionally to determine the completion of the distillation; these tests may be physical or chemical, depending on the nature of the substance. For theoretical discussion see Textbooks on Physical Chemistry.

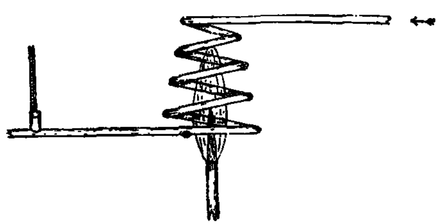


FIG. 15.

**Superheated Steam.**—This is used for distilling substances which are difficultly volatile. The steam from the generator is passed through a copper spiral (Fig. 15) which is heated by a Bunsen flame, and which has a side tube attached for a thermometer. This tube is placed on the exit tube, and as far away as possible from the flame.

**Continuous Steam Distillation.**—The apparatus (Fig. 16) is very convenient when this process has to be carried on for some time. The substance to be steam distilled is placed in the round-bottomed flask A along with water if none is present. To the flask is attached through a cork a tube delivering to a vertical tube B, and with a small side tube C. A

condenser is fitted to the top of the vertical tube and a receiver D of the type shown or a flask with a two-holed stopper. The small side tube C is attached to a delivery tube E fixed to the receiver by means of a rubber tube. The capacity of D must, of course, be less than the volume of liquid in A. When the flask is boiled the vapour is condensed in the condenser and the liquid falls into the receiver. When this process has been continued for some time, the top layer of water in the receiver gradually rises, and when it reaches the level of the small side tube C passes back automatically into A. The process is now continuous. The liquid in the receiver can be separated when desired by opening the tap on the bottom of the receiver.

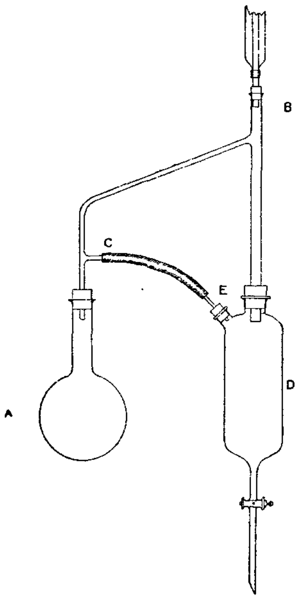



FIG. 16.

When the liquid to be steam distilled is lighter than water, the small glass tube E is extended to the bottom of the receiver.

## Dry Distillation

This is a process which is occasionally used in the laboratory; it is usual to perform the distillation in an iron or copper vessel as glass will not stand the heat. In order to prevent a cake forming, and thus secure uniform heating, it is advisable to mix the substance to be distilled with iron turnings which conduct the heat into the interior of the mass, provided, of course, that the iron turnings have no chemical action on the substance.

## Vacuum Distillation

Some liquids decompose when distilled in the ordinary way; these can generally be distilled under reduced pressure. The apparatus used is shown in the sketch (Fig. 17) and may be of glass, provided large vessels are not used. It is usual to heat the distilling flask in a bath and not by direct heat. The distilling flask, which may be of the ordinary type or, better, having two necks (Figs. 18, 18A), should be wrapped in asbestos cloth, which acts as a protection as well as a preventative of loss of heat by radiation. To the flask is attached a glass tube drawn out to a fine capillary which dips below the surface of the liquid. By the passage of small quantities of air, or some other gas if air is unsuitable, regular boiling is maintained, and this is of extreme importance. A rubber tube with screw clip may be connected to the top of the capillary tube so as to regulate the air supply. Provided the liquid has no action on rubber, rubber stoppers should be used; they should be smeared with vaseline before inserting. Good corks, however, are quite satisfactory if covered with collodion or

cellulose acetate solution after insertion, or charred, as described on p. 8. Between the receiving flask and the pump is placed a manometer for reading the pressure. If a water pump is used a water trap (Fig. 19)

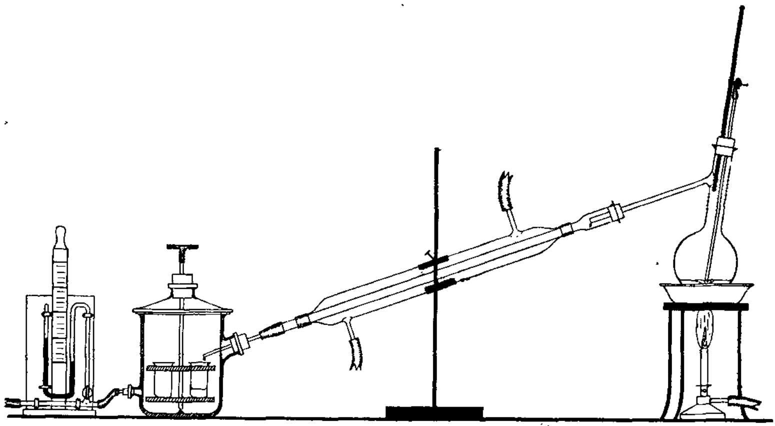


FIG. 17.

must be inserted between the pump and the manometer to prevent water sucking back. When the distillation is to be discontinued the flame should be extinguished and air allowed to enter by carefully opening the tap attached to the water trap.

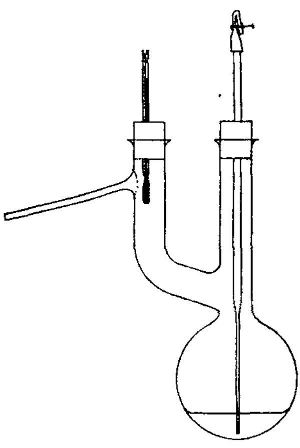


FIG. 18. (Claisen.)

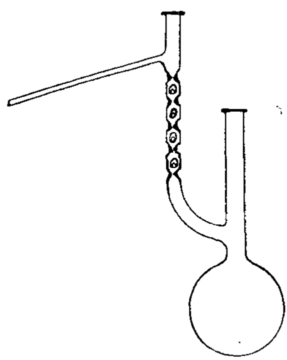


FIG. 18A.

Vacuum distillation may be used in fractionating liquids. The apparatus is similar except that facilities are provided in the receiving vessel for collecting different fractions. Two sketches (Figs. 17, 20) show suitable types of receivers for use in fractionating under reduced pressure. The desiccator type is shown in Fig. 17, and contains six or seven small

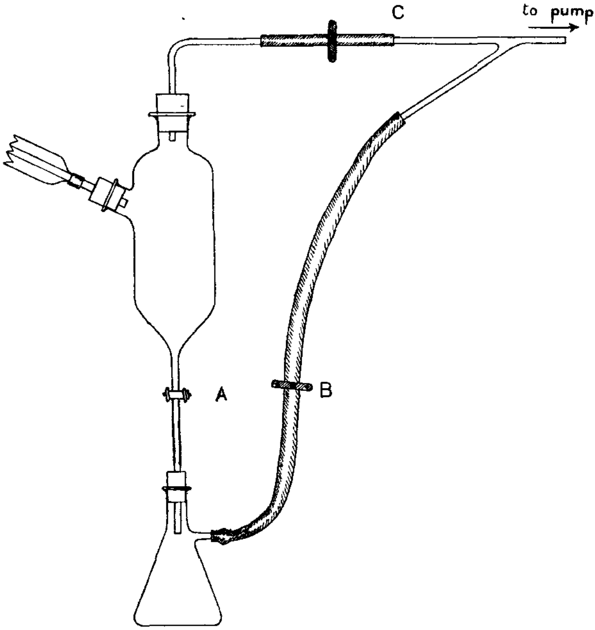



FIG. 20.

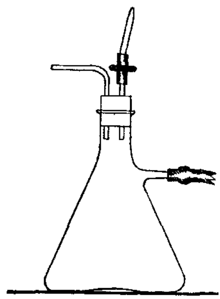


FIG. 19.

receivers into which the distillate can be run, different fractions being obtained by turning the handle on the top, thus bringing another receiver into position. This avoids breaking the vacuum. Fig. 20 shows a single receiver which can be emptied without breaking the vacuum. While a fraction is being collected, A and B are closed while C is open. The receiver is emptied by closing C and opening A and B. While the next fraction is being collected the receiving flask may be removed.

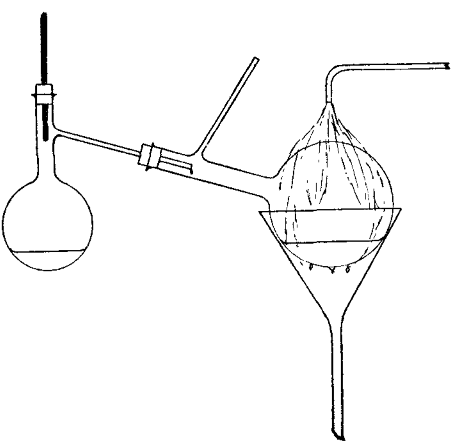


FIG. 21.

It sometimes happens that a liquid "bumps" violently even with the addition of a few porcelain clips and the passage of a fine gas current through the flask. The best plan in such cases is to immerse the flask so far into the heating bath (see p. 38) that the level of the latter is above the level of the liquid in the flask. In this way the vapour is superheated, and bumping does not occur.

A convenient apparatus for distilling liquids of high boiling

point under reduced pressure is shown in Fig. 21, in which the receiver is an ordinary distilling flask, and is kept cool by a current of cold water (for another type of receiver see Fig. 23).

A cylinder, fitted at one end with a good cork and drawn out to a tube at the other, may be packed with test tubes and used in such a manner as to function as a fractional receiver by rotation of the cylinder as required. An adapter passing through the cork delivers the distillate into the test tubes. The pump is attached to the drawn-out end of the cylinder.

As with glass flasks there is a risk that they may collapse under a vacuum, especially when heated to high temperatures, the eyes should be protected by goggles and "safety glass" screens employed.

## Pressure Condenser

The apparatus (Fig. 22) is convenient to use when it is desired to distil at ordinary pressure or *in vacuo* a solid of high boiling point which would solidify in an ordinary condenser, *e.g.*, α- or β-naphthol, or benzidine.

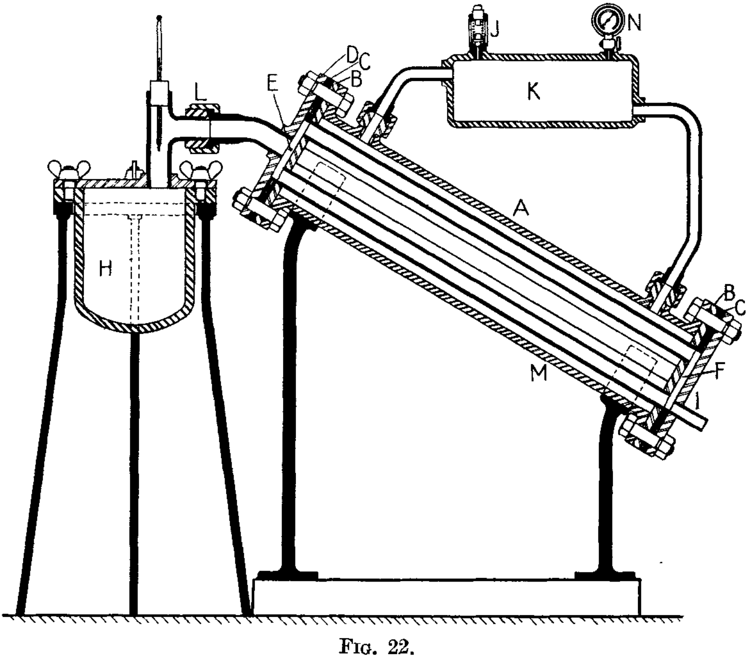



FIG. 22.

The condenser, made of steel tubing, consists of a 4-inch diameter outer jacket A, surrounding 4 or 6 tubes of ½-inch diameter expanded into the plates B. Plate C is in the form of a flat ring, while to plate D is attached the delivery tube from the cast-iron still H. The chamber E then serves as a receiving chamber for the vapours. Similarly, chamber F acts as a delivery chamber for the condensed liquid, which then flows out

to a receiving flask in the form of an ordinary distilling flask at the exit tube I. The condenser is filled with water at the removable safety valve J, which has previously been set to " blow off " at any desired pressure, say, 80 lbs. per square inch. The safety valve is replaced on the reservoir K and the still firmly screwed to the condenser by the movable nut L.

The substance to be distilled is placed in the still, and the lid screwed tight by means of the thumb screws, a suitable jointing material being used between lid and pot. The condenser is then heated by a Bunsen at M and when boiling point has been reached, pressure begins to be recorded on the pressure gauge N. The table below gives the temperatures corresponding to various pressures. When the required pressure has been registered on the pressure gauge, the still H is heated.

An electric vacuum pump is attached, through the usual traps, to the glass receiving flask. The substance distils when the boiling point is reached, as shown on the thermometer, and may solidify on entering the flask, but by the application of heat it can be delivered to the bulb of the flask before it solidifies.

| Pressure lbs. sq. in. | Temperature °C. | Pressure lbs. sq. in. | Temperature °C. |
|---|---|---|---|
| 0 | 100·0 | 30 | 134·4 |
| 5 | 108·4 | 40 | 141·1 |
| 10 | 115·0 | 50 | 147·7 |
| 15 | 121·1 | 60 | 152·7 |
| 20 | 126·1 | 70 | 157·7 |
| 25 | 130·5 | 80 | 162·2 |

**Pumps.**—The pressure obtainable by a good water pump is approximately the vapour pressure of water at the temperature (10—15 mms.). For pressures below this a mechanical pump must be employed, which in some cases reduces the pressure to less than 1 mm.

*Note.*—The boiling points at atmospheric pressure of high boiling liquids are reduced by about 100° at 10—15 mms.

**A Receiver for Distillation in a Current of Gas or under Reduced Pressure.**—The receiver shown in Fig. 23 can be used to fractionate liquids in a current of gas or under reduced pressure.

The condensing liquid is first collected in A, the tap B being turned so as to connect tubes *b* and *c*. The gas current meanwhile passes from A into C, where it displaces air and prepares C for the reception of the fraction. The tubes *d* and *e* are shown as for a heavy gas, *e.g.*, $CO_2$; for a light gas the relative depths to which they enter the flask must be reversed.

To isolate the fraction, B is turned to put *c* in communication with A. The liquid, helped by the gas-current, passes into C, B is turned through 180°, and the tube *c* swept out by gas passing from *b*. Taps D and E are

closed, and the ground-glass joint F opened. A new flask is put on at the joint, and when the air in it has been swept out, the next fraction can be collected. If it is necessary to collect the fractions at very short intervals, several flasks can be swept out simultaneously by connecting them in series to *f*. If glass joints are unnecessary throughout, pieces of rubber tubing can be used for connecting the flasks together.

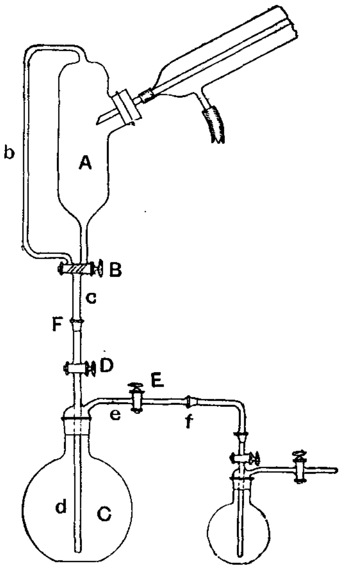



FIG. 23.

As shown, the apparatus is adapted for the collection of very readily oxidisable liquids. In many cases it will not be necessary to have taps D and E; and F can be replaced by a rubber connection. The apparatus can also be used for fractionation *in vacuo*. The vacuum pump is connected at *f*, and while a fraction is collecting, exhaustion takes place from *b* to *c*. The fraction, after being sucked into C by turning B through 180°, is isolated by closing B by a right-angle turn, closing E and disconnecting at *f*. Air or other gas can then be admitted through E, and F disconnected. If preferred, E can conveniently be a three-way tap. Another flask is then fitted on, and when exhausted, *b* and *c* are put in communication. To save time, several flasks can be kept exhausted by attaching them in series to *f* and to the pump (J. S. C. I., 41, 59 (T.) ).

## Sublimation

Sublimation is a process used for the purification of some compounds, especially when the quantity of substance is small. The first point to determine is that the substance does actually sublime. This is done by heating a little of the substance in a dry test tube held in an almost horizontal position. The sublimate, if any, will collect on the colder parts of the tube.

Several types of apparatus are available for sublimation. If the substance sublimes readily, the following apparatus is convenient. It consists of two watch-glasses clamped together by a brass clip, the substance being placed in the lower glass and a perforated filter paper between them. The sketch (Fig. 24) shows the arrangement. This is heated on a sand bath. The

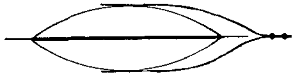


FIG. 24.

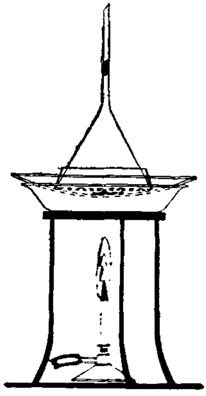


FIG. 25.

sublimate collects in the upper glass, and the filter paper prevents the sublimate from falling into the residue. The upper watch-glass may be kept cool by covering it with several pieces of damp filter paper and wetting these from time to time. The upper watch-glass may be replaced by an inverted glass filter funnel with a plug of cotton wool in stem (Fig. 25). It is desirable to support the filter paper with a porcelain ring.

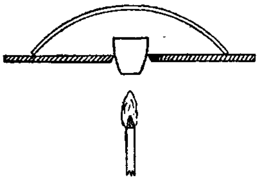


FIG. 26.

When the substance is difficult to sublime, it may be heated in a crucible placed in a round hole in a piece of asbestos board. The crucible is covered with a large clock-glass and a small flame is used so that the heat is directed only on to the crucible, as shown in Fig. 26.

## **Filtration** (see also p. 10)

Filtration by means of suction is generally employed where possible in the operations of organic chemistry, since more rapid and more complete separation of the mother liquor is in this way effected. For this purpose several types of apparatus are in use. For large quantities of material the Buchner funnel and flask (Fig. 27) are used, the filter paper being cut

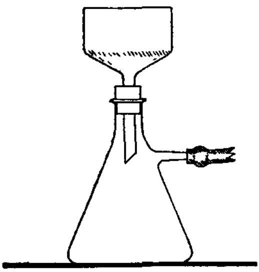


FIG. 27.

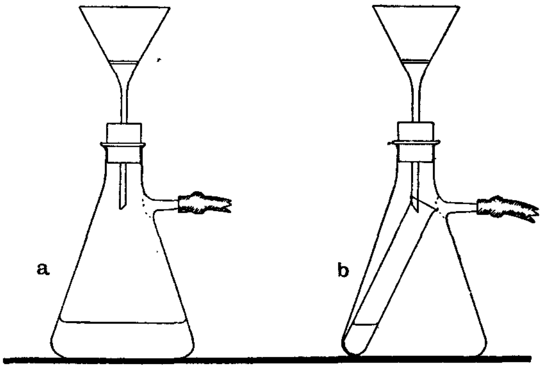



FIG. 28.

to cover the perforations. If filter paper is attacked by the liquor, cloth, such as flannel or cotton, might be used instead. For highly corrosive liquids, a layer of fibrous asbestos should be employed as filtering medium; this is prepared by boiling asbestos wool with hydrochloric acid, then pouring on to the Buchner funnel and washing thoroughly with water while suction is applied. If necessary, the asbestos is then dried by washing successively with alcohol and ether. In all cases the filtering medium should be moistened with the solvent used, and well pressed down on the perforated plate.

An ordinary funnel in which is placed a perforated disc (Fig. 28a) may

be used instead of the Buchner funnel, and this form is very convenient for separating small quantities of solids. The paper should be cut slightly larger than the disc, and should be carefully placed in position, and pressed down after moistening.

For separating small quantities of liquid the apparatus (Fig. 28b) is very suitable; the liquid is received in a test tube placed inside the Buchner flask.

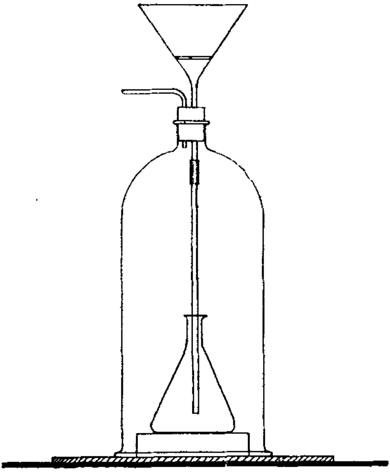


FIG. 29.

The apparatus (Fig. 29) shows the most convenient arrangement when the filtrate is further required. It consists of a bell-jar cemented with vaseline to a ground-glass plate; the double-holed rubber stopper carries the filter funnel and a tube for connecting to a pump. The liquid is collected in a receiver placed inside the bell-jar. The great advantage of the apparatus is that any type of receiver may be employed. If the filter funnel has a long stem, it may be used in conjunction with a hot-water jacket (Fig. 3) or an ice jacket (Fig. 4).

In order to separate as much liquid as possible from a large bulk of solid, the latter, after being filtered in the ordinary way by means of a Buchner funnel and well pressed, is removed from the funnel, placed in a stout piece of cloth and tightly wrapped. It is then placed in a press of the ledger type and pressure gradually applied.

## Decolorisation

It often happens that the compound prepared in a particular preparation is discoloured; various methods are used to remove traces of colouring and of tarry matter. The most common is to boil up the substance in solution with animal charcoal—added in the cold—and then to filter and recover the compound from the filtrate by crystallisation or distillation. Very little of good decolorising carbon is necessary as a rule, and that may be revivified by impregnating with a concentrated zinc chloride solution, igniting, and washing with acid. It should be remembered that animal charcoal contains only about 10% of carbon, the remainder being phosphates of different metals, iron, etc.; this should be considered especially when decolorising in acid solution. If any of these substances are likely to be harmful, the animal charcoal should be boiled up with hydrochloric acid, filtered, washed and dried. Sometimes a solution remains cloudy after filtration. As a rule this cloudiness can be removed by adding very small equivalent quantities in solution of calcium chloride

and sodium phosphate. The calcium phosphate precipitated usually brings down all gelatinous matter and may then be removed by filtration.

Discoloration is sometimes due to oxidation, and the colouring matter may often be removed by passing $SO_2$ gas through the solution, always provided that this has no action on the substance.

Cloudiness, colouring matter, etc., may also in some cases be removed by the use of the Stream-line filter (J. S. C. I., 45, 660). It is important however, in the use of this filter, that the rate of filtration should be low.

## Salting Out

Some substances which are soluble in water are not soluble or only slightly soluble in solutions of certain salts, such as sodium chloride, calcium chloride, sodium acetate, sodium sulphate. The salt may be added in the solid form or as a saturated solution. By this means alcohol and acetone can be separated from their solutions in water.

The process is used very largely on the technical scale for the separation of dyestuffs (see pp. 380, 381).

## Extraction of Solids

When it is required to separate a solid from an impurity, it is desirable to carry out the extraction in a Soxhlet apparatus, a sketch of which is shown (Fig. 30). The substance to be extracted is placed in a paper thimble A which is set in position in the main Soxhlet tube, a loose plug of cotton wool being placed in the top of the thimble. The Soxhlet is attached to a flask B containing a small amount of a solvent; the solvent chosen should be such that either the desired substance or the impurity is insoluble, or nearly so. A condenser is attached to the Soxhlet tube; the ball condenser C shown in sketch is the most convenient.

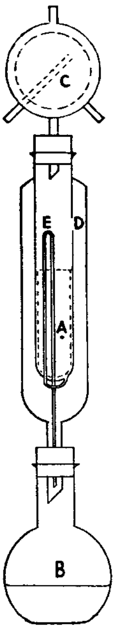


FIG. 30.

When the solvent is boiled, the vapour passes through opening D to the condenser, from which liquid drops back to the thimble. When this liquid reaches the top of the side tube E, it automatically syphons back into the flask B with the extracted matter in solution. The process is continuous.

It is advisable to use a minimum quantity of solvent at the beginning and, if necessary, to add more solvent through the condenser. More rapid extraction can be brought about if the substance is intimately mixed with some inert substance, such as glass or sand.

When the extraction is judged to be complete, the Soxhlet is removed and the substance crystallised from

the solution remaining in the flask. For modifications, see J. S. C. I., 43, 281; 50, 144.

### Separation of two Immiscible Liquids

Funnels of the types shown in Fig. 31 are used. The liquids to be separated are run into the funnel, and after standing for some time the stopper at the top is removed and the more dense liquid is run off through the tap at the bottom. If the upper layer is required, it is poured out through the top of the funnel after running off the bottom layer; this is to prevent contamination with the liquid in the stem and tap of the funnel. In all cases a funnel of convenient size should be chosen.

If the volume of liquids is small, separation can be effected by the use of a small pipette, to which is attached a length of rubber tubing; the rubber tubing is held in the mouth, gentle suction is applied, and the eye kept on a level with the common surface of the liquids.

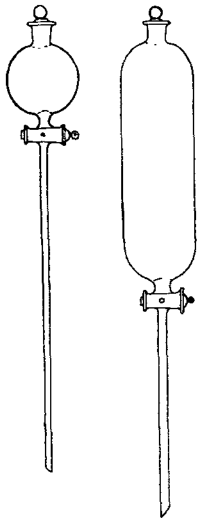


Fig. 31.

**Separation by Extraction.**—Separating funnels are again used for this purpose. The substance to be extracted is generally in solution or suspension in water. A solvent which is immiscible with water and in which the substance is soluble is added—in small quantities at first. The funnel is stoppered and agitated, holding the tap and stopper closed, after which it is set aside in a vertical position until the liquids separate. Separation is then effected as above. The solvent most commonly employed is ether, but benzene, chloroform, ligroin and amyl alcohol are used in special circumstances.

In all cases extraction should be carried out more than once, the extracts being added together. The amount of substance which goes into solution in ether, etc., depends on the distribution coefficient, that is, the ratio of the concentrations in the two solvents after equilibrium is attained. This ratio is constant for any given temperature, provided the molecular weight of the solute does not vary in either solvent (see "Physical Chemistry," by A. J. Mee). It follows then that extraction may have to be repeated several times, and also that it is more efficient to extract a number of times with successive small quantities of solvent rather than once with a large quantity.

When a quantity of the substance separates from the solution as an oil, this oil should be separated before extraction is attempted.

In extraction with ether the following points should be noticed:—

1. All burners in the immediate vicinity should be extinguished.
2. After shaking, the funnel should be inverted and the pressure released by gradually opening the stopcock.

3. If an emulsion persists after standing, this may frequently be destroyed by agitating the ethereal layer with a glass rod. Addition of a few drops of alcohol is sometimes effective. In special cases filtration may be useful. If the funnel be held in a stream of warm water for a time, separation may be facilitated.

4. Extraction is complete when a sample of the ether layer evaporated to dryness leaves no residue.

5. Ether is soluble in water to the extent of 8%. If the aqueous volume to be extracted is large, it should be saturated with common salt, in which solution ether is much less soluble.

6. Water is soluble in ether to the extent of 1·5%. It follows, therefore, that the ether extract must be dried (see p. 37) before removing the ether by evaporation.

7. The ether is generally removed by distillation. A moderate sized flask should be used and more solution added from time to time. The apparatus shown in Fig. 32 enables the additions to be made without interruption of the distillation. The flask is fitted with a two-holed stopper carrying a dropping funnel and a glass tube. By means of a piece of rubber tubing and a second short piece of glass tubing inserted through a cork, the top of the funnel is connected through the first piece of glass tubing with the interior of the flask; the rubber tubing on this connection carries a spring clip. The ethereal solution —a portion at a time—is placed in the funnel and the cork inserted in the neck of the funnel. The stop-cock of the funnel and the spring clip are then opened simultaneously, and the ether flows into the flask without interruption, since the pressure above the ether in the funnel and the pressure inside the flask have been equalised by the opening of the spring clip. When the ether has run in, the tap and the clip are closed.

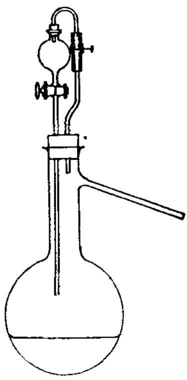


FIG. 32.

8. Salts are generally insoluble in ether. Ferric chloride, mercuric chloride, mercuric iodide, stannous chloride and chromic anhydride, however, are fairly soluble.

## Drying

**Drying of Solids.**—(*a*) *At Ordinary Temperature.*—When the solid is insoluble in a volatile solvent, such as ether or petroleum ether (40°—60°), and this solvent is miscible with the solvent from which the solid was crystallised, drying may be greatly facilitated by washing the substance while still on the filter with such a volatile solvent. The usual method of drying at ordinary temperature consists in spreading the solid on several layers of filter paper or on a porous plate, and leaving until dry. It is necessary, however, to protect the solid from dust contamination by covering with filter paper or watch-glass in such a manner that free access

of air is permitted. The drying may be more quickly carried out by placing the solid on a porous tile in a vacuum desiccator.

*Desiccators.*—These are of two types, the ordinary and the vacuum (see Fig. 33). The drying in the latter is generally 6—7 times quicker than in the former. The desiccator is charged, according to the nature of the substance to be absorbed, with one or other of the following substances.

Conc. sulphuric acid : to absorb water, basic substances.
Granular calcium chloride : to absorb water, alcohols, some basic substances.
Solid sodium or potassium hydroxide: to absorb water, acids, phenols, alcohols, esters.
Quicklime : to absorb water, acids.
Soda lime : to absorb water, acids.
Paraffin wax : to absorb carbon disulphide, ether, chloroform, benzene.

It is obvious from the foregoing list that impurities as well as solvent may be removed from a solution by exposure in a desiccator containing a suitable absorbent. It is essential that the absorbent does not react with the substance to be dried.

*N.B.*—A suction flask should always be inserted between a vacuum desiccator and a water pump when the latter is used, as slight variations in water pressure may result in water being sucked back into the desiccator.

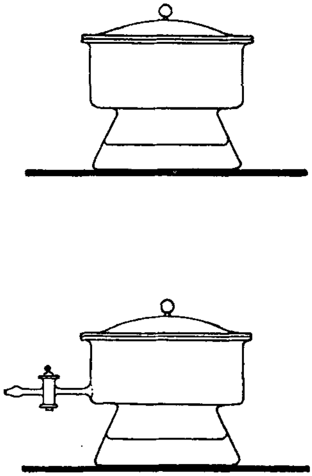


FIG. 33.

(*b*) *At Higher Temperature.*—If it is desired to dry a solid at a temperature higher than ordinary, a test should first be made with a small portion. This is necessary since many substances decompose at relatively low temperatures and *such temperatures should be noted.* Moreover, the presence of slight impurities or of solvent may considerably lower the melting point of the solid. Other changes—loss of solvent of crystallisation, etc.—may take place on heating, and these should be noted.

For drying at temperatures up to 100°, the water bath or steam oven is generally used. For drying at higher temperatures the air oven is employed, but here a thermometer should be inserted and particular care taken that the substance is not over-heated. A very convenient form of drying apparatus is the toluene bath (p. 38).

**Drying of Liquids.**—(*a*) *At Ordinary Temperature.*—Liquids are usually dried by the addition of some solid dehydrating agent, such as granular calcium chloride, solid caustic potash or soda, anhydrous sodium sulphate, anhydrous potassium carbonate, anhydrous cupric sulphate, phosphorus pentoxide, metallic sodium. It is essential that the drying agent should have no action on the liquid, or on any substance dissolved in it, and great care should be exercised in the choice of a drying agent. For example,

calcium chloride should not be used for drying alcohols or amines. Caustic potash or soda should not be employed for drying acids, phenols, esters, certain halides, etc. The minimum quantity of drying agent should be used, otherwise liquid is lost by absorption. After standing some time, the liquid is separated by decantation or filtration.

The drying of ethereal solutions is an operation frequently met with. In most cases it is advisable to dry an ethereal extract before evaporating off the ether. Again, to dry a moist solid, it is often convenient to dissolve it in ether and to dry the ethereal solution with a dehydrating agent. The dry solid is then obtained by evaporation. For the drying of organic liquids by dialysis, see U. S. P., 1,885,393.

(*b*) *At Higher Temperatures.*—This method is seldom employed, and is only effective when the liquid has a high boiling point and is not volatile in steam.

### Baths

Baths are used for heating, drying, etc.; the heating can be thus carried out more uniformly than is possible with a direct flame. A judicious selection of the type of bath required for any operation should be made—an air bath should not be used if a water bath suits the purpose. In all cases a means of ascertaining the temperature should be provided, either by taking the temperature of the bath, or of the substance heated on the bath.

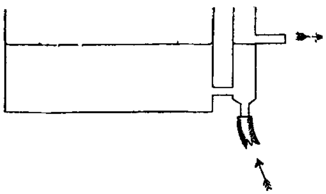


FIG. 34.

**Water Bath.**—This is employed for heating or drying up to 100°. For temperatures below 100° the vessel should be immersed in the water; for 100° the vessel should be so far immersed as to be largely surrounded by steam. When a water bath is to be used for many hours, a constant-level arrangement is attached (Fig. 34).

**Salt Solutions.**—Temperatures above 100° can be attained by the addition of salts to the water. The boiling points of a few saturated solutions are appended:

| | B.P. |
|---|---|
| Sodium chloride | 109° |
| Magnesium sulphate | 108° |
| Potassium nitrate | 116° |
| Sodium nitrate | 121° |
| Calcium chloride | 180° |

**Toluene Bath** (Fig. 35).—This bath consists of a double-walled enclosure, access to which is obtained by a hinged door carrying a stout rubber joint. The door is fastened by thumb-screws. Any suitable liquid can be placed in the outer jacket to which is attached a condenser; the liquid, however, most generally used is toluene (B.P. 110°). The inner compartment

is fitted with an exit tube carrying a vacuum gauge, and this may be attached to a vacuum pump. This offers a very convenient method of drying substances at a temperature slightly above 100° and under reduced pressure.

**Air Bath.**—A convenient form of air bath is made of sheet iron, and completely lined on the outside with asbestos. Air ovens are generally used for temperatures above 100°. In no case should the substance be placed on the lower shelf; the bulb of the thermometer should reach close to the shelf on which the substance is placed.

**Sand Bath.**—This form of bath is used for temperatures well above 100°. A thermometer should always be placed in the substance being heated. It is important that the layer of sand should only be just thick enough to protect the vessel from excessive heat.

**Oil Bath.**—Suitable oils may be used such as higher boiling paraffins, melted paraffin wax, glycerine, etc. The oil should not be heated to its flash point, and the surface of oil exposed should be as small as possible.

**Graphite Baths.**—These are sometimes used in place of oil baths.

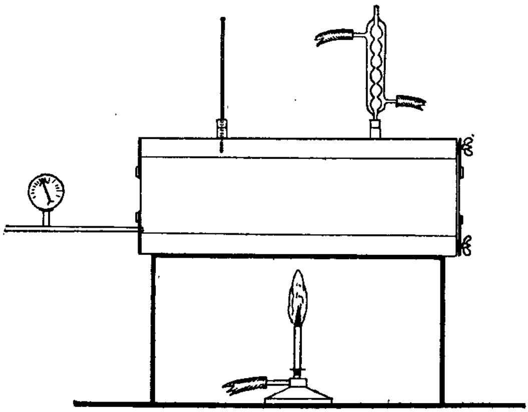


FIG. 35.

**Metal Bath.**—This type of bath is the most suitable for heating to high temperatures. Before heating, the vessel should be held in a luminous flame until covered with a deposit of carbon which prevents the fused metal from adhering to the flask; it also renders the vessel less liable to crack.

The following metals and alloys may be used :—

**Bi** (4), **Cd** (1), **Pb** (2), **Sn** (1), M.P., 65°; **Bi** (3), **Pb** (2), **Sn** (2), M.P., 95°; **Pb** (37), **Sn** (63), M.P., 183°.

The last-mentioned alloy, which is the eutectic mixture of lead and tin, is very convenient for many operations (see p. 210). When used in a pot of the type shown in Fig. 53 oxidation of the metal—a drawback attending the use of metal baths—is largely overcome.

## Mechanical Agitation

The importance of mechanical agitation cannot be over-estimated. In some preparations a yield cannot be obtained at all unless efficient agitation is provided; mechanical agitation should be used, therefore, wherever continuous agitation is essential. A suitable vessel should first

be chosen, and an agitator made, usually of glass rod, to suit this particular vessel. The relative densities of the substances to be mixed must be borne in mind; obviously it will require much more vigorous agitation to sulphonate benzene, or to reduce nitrobenzene with, say, iron, than to fuse a sulphonic acid with caustic soda—due to the much greater differences in the specific gravities of the reacting substances. The propeller type of agitator is always serviceable provided the speed is high. The driving force may be electric or hydraulic, but various simple devices can be adopted depending on the nature of the chemical reaction. For

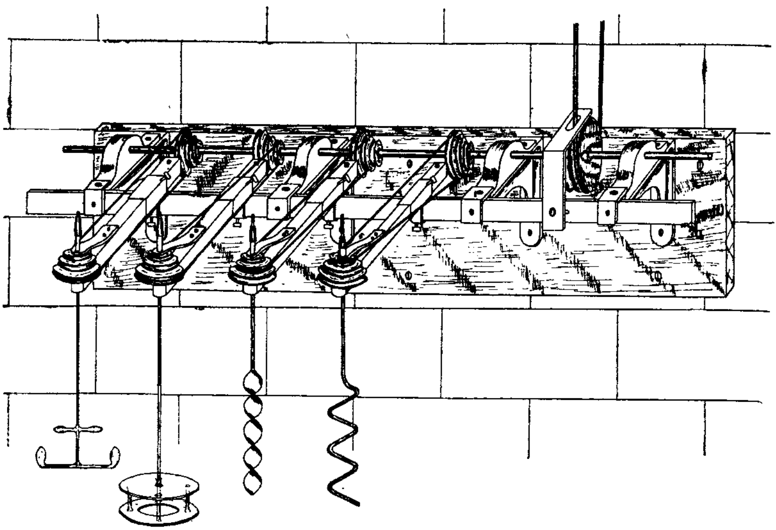


FIG. 36.

example, air, steam or other suitable gas may be passed into the mixture, etc.

Where active boiling is taking place in a mixture, mechanical agitation is usually unnecessary.

The sketch (Fig. 36) shows a battery of agitators driven by an electric motor and employing different types of agitators. By changing the driving belt to different pairs of pulleys, different speeds of agitator can be obtained. It is always wise to have some idea of the speed of agitation.

**Sulphonation Pot.**—The most satisfactory method, however, of using mechanical agitation is in conjunction with a specially constructed piece of apparatus. Various types can now be procured, and some are very effective. Fig. 37 shows one such. It consists of a cast-iron pot with a lid carrying the brass bearing and gear wheels of the central shafts. The large driving pulley drives the outer shaft in one direction and the inner shaft in the opposite direction, a suitable form of " blade " being attached to each. The lid is attached to the pot by thumb-screws, suitable jointing matter being used, such as rubber. Openings are provided in the lid for

reflux condenser, thermometer, and addition tube. The apparatus, which may be driven from an electric motor, is admirably suited for sulphonations, nitrations, and reductions. When such an apparatus cannot be obtained the apparatus (Fig. 38) in glass is recommended.

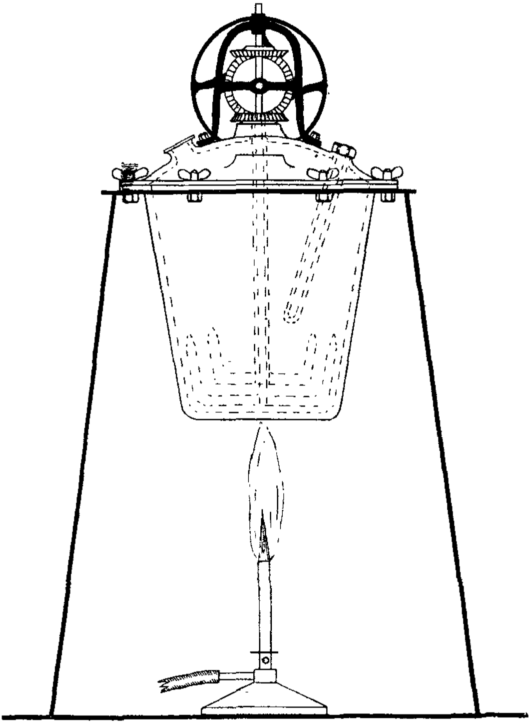


FIG. 37.

### Heating under Pressure

When a mixture of substances is heated in an enclosed space no volatile matter can escape, and hence, at a certain period in the heating, pressure begins to develop. Substances or solutions may thus be heated to a temperature above the boiling point of any or all of them without incurring the loss of reacting substances or reaction products; and the method has the advantage that many reactions which cannot be brought about by boiling substances in open vessels can be easily brought about by heating under pressures above atmospheric. If it is desired to heat two substances under pressure, but not to a temperature above the boiling point of either, a third substance of lower boiling point which has no chemical action on either of them is introduced.

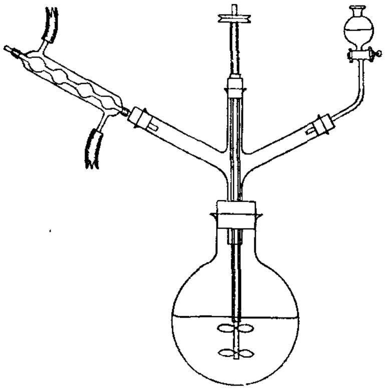


FIG. 38.

Heating under pressure is generally done in—(*a*) Sealed Tubes, or (*b*) Autoclaves.

(*a*) **Sealed Tubes.**—As only small quantities of substance can be dealt with, the method is only applicable for small scale experiments or quantitative work (*e.g.*, Estimation of Halogens—Carius). Generally, soft glass tubes about 50 cms. long, 18—20 mms. outside diameter, and walls

2·5—3 mms. thick, are used, but if the contents attack soft glass, or if large quantities of gas are evolved on heating, or if the temperature of heating is high, tubes of difficultly fusible potash glass should be employed, since these are more resistant to chemical action and do not crack so readily. As glass deteriorates with age, a piece of new glass should be selected for sealed tube work. A suitable length is cut (see p. 460), thoroughly washed, and after being allowed to drain for some time is dried by warming with a moving flame while a current of air is blown through it.

To seal one end of the tube, about 2 inches of the tube at this end is heated by revolving it in the smoky flame of a blowpipe for a few minutes. The blast is then turned on slowly, and the tube, while held in one hand at an angle of 45°, heated at the end, until softening takes place, when a previously warmed glass rod held in the other hand is fused on to it. The blast flame is adjusted so that it will heat a zone of glass about as broad as the diameter of the tube to be sealed, and is directed at a point about 3 cms.

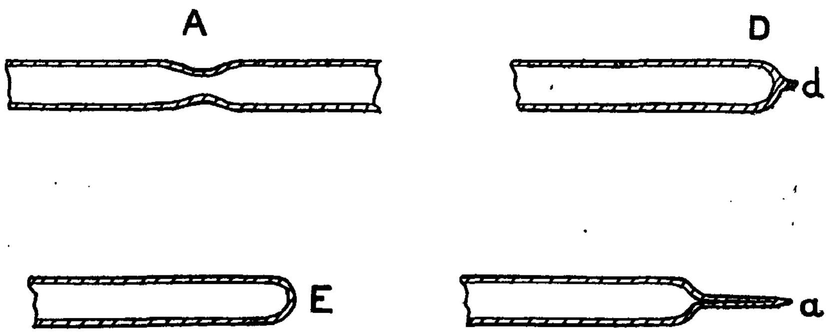



Fig. 39.

from the end of the tube, which is slowly brought into the flame with constant rotation. When the glass begins to thicken the ends are slowly drawn out, care being taken not to extend the softened glass too much, but to allow the sides to fall together, as shown at A (Fig. 39). When this occurs, the narrow part is heated till it melts and the ends pulled asunder. The closed end should present the appearance shown at D. If a considerable mass of glass be left at *d*, it may be removed by heating it to redness, touching it with the pointed end of a cold glass tube, to which it will adhere, and by which it may be pulled away. Any blob of glass remaining is heated in a small blowpipe flame, and by gently blowing with the mouth into the open end of the tube, and re-heating and blowing again, the blob can be removed, and finally, by using a rather larger flame, heating and blowing alternately, the end is neatly rounded—shown at E. After cooling slightly the hot end of the tube is annealed by holding it for a few minutes in a luminous flame.

Hard glass is much more easily worked in the oxygen-coal gas flame, obtained by attaching a cylinder of oxygen in place of the air blast to the lamp.

*Filling the Tube.*—Since the tube is afterwards sealed at the open end, it is necessary when filling the tube to take care that none of the ingredients come into contact with it near that end. The tube should be clamped in a vertical position beside the working bench, and a funnel tube, having a stem as wide as the tube will admit, is inserted in the open end; through this the substances are added. In analytical work (see Estimation of Halogens) the weighed substance should be introduced in a container of its own. When fuming liquids are employed (see Preparation of Paranitrobenzyl Bromide) these should be placed in test tubes stoppered with glass wool or asbestos; obnoxious fumes during the sealing process are thus largely avoided. When withdrawing the funnel tube, care is taken to avoid bringing it into contact with the walls of the tube. The amount of substance which may be introduced depends on the conditions; the tube should never be more than half full, and if much gaseous product is formed, or if the temperature of heating be high, a lesser quantity should be introduced.

*Sealing.*—The tube is held at an angle of 45°, and in a manner already described; the open end is warmed in a smoky flame, then heated to softening, and a glass rod sealed on to it. Likewise, as described before, the tube is heated at a point about 3 cms. from the end by rotating it in a blast flame. The glass is evenly heated and not drawn out, but when the apparent inside diameter of the tube is reduced to about 3 mms., the tube is quickly withdrawn from the flame and a capillary formed by slowly drawing out the thickened part (Fig. 39). In order to secure a thick end to the point of the capillary *a*, about 2 cms. of the tube at the shoulder is warmed a little at the moment of finally sealing it; the contraction of the air in the tube, in consequence of its cooling, ensures the glass at *a* running together to a solid end when it is melted in the flame. If it is desired to collect a gas produced during the chemical reaction, the capillary is made several inches long, and is bent into the form of a delivery tube. It is then possible to break the tip of this under a cylinder in a trough of liquid.

*Sealing of Hard Glass.*—For this a slightly different method of sealing is employed. As soon as the glass is sufficiently soft, it is not thickened, but is drawn out at once to a wide capillary. By directing the flame on the shoulder of the tube and continuing to draw out the capillary is then lengthened to about 3 cms. It is then thickened by revolving in the flame and finally sealed off. The sealing of hard glass requires at least a first-class blowpipe; and the sealing may be facilitated by placing a brick or tile near the flame in such a position that the heat is reflected on to the tube.

As soon as the tube is sealed and annealed, it is clamped in a vertical position, with capillary uppermost, and left to cool in a place where if it bursts no damage will accrue.

*Tube Furnace or Bomb Furnace.*—When cold, the tube is transferred to the removable metallic cylinder of the tube furnace (Fig. 40). The cap of the cylinder is screwed on and the latter placed in position in

the furnace. Various forms of furnace are used: the common forms are heated by a series of pinhole gas-jets, and are easily regulated. The removable cylinder is not supplied with all furnaces, but it is advisable to have it for the following reasons: (*a*) The furnace may be approached without fear of glass splinters, and (*b*) in case the tube bursts, the glass fragments and contents (of the sealed tube) remaining in the cylinder can be easily removed.

When a removable cylinder with screw cap is not available, the sealed tube is placed in the fixed cylinder of the furnace, the capillary end pointing towards a wall of the furnace room so that no damage will accrue in case of an explosion.

At the commencement of the heating, small flames are used and the temperature raised gradually to the desired point. The temperature is indicated by a thermometer, inserted through a cork in the opening at the top of the furnace, the bulb of the thermometer being placed level with the iron tube. The danger of the bursting of sealed tubes may be diminished in many cases by interrupting the heating after a certain length of time, opening the capillary after the tube has completely cooled, and allowing the generated gases to escape. The tube is then resealed and heated again. Or, to take an example of bromination, one-half the necessary quantity of bromine may be added at first, the tube sealed and heated to the desired temperature; the tube is then allowed to cool, after which the capillary is opened, the second instalment of bromine added through a long capillary tube, and the tube after being resealed is heated as before.

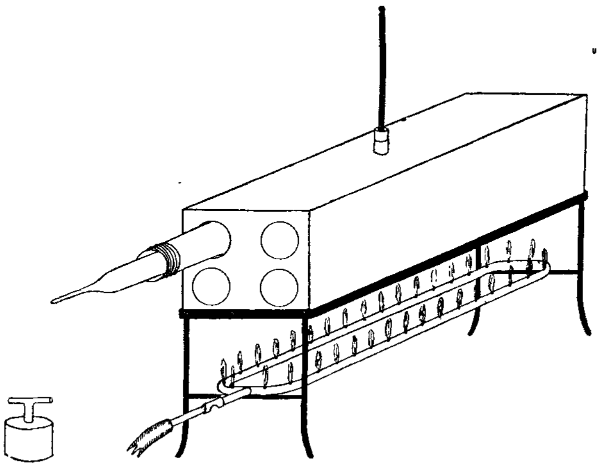


FIG. 40.

*Opening Sealed Tubes.*—The greatest possible care must be observed in handling an unopened tube. It must never be removed from its protecting case for examination or for any other purpose. It must not be opened until perfectly cold, and when being opened it is held in such a position that no one can be injured should it burst.

When cold, the protecting case of iron is withdrawn from the furnace and held in one hand. The cap (if present) is unscrewed, and while the iron tube is held in a slightly inclined position so that the capillary is somewhat higher than the other end, the capillary is made to project

beyond the iron case by giving the cylinder a slight jerk. The part of the iron cylinder near the open end and which is gripped with the hand is wrapped round with a cloth. The extreme end of the capillary is then gradually heated in a Bunsen flame. If pressure exists inside, the end of the capillary is blown open on softening, provided there is no obstruction in the capillary. If there is obstruction it may be removed by heating.

Under certain conditions, as, for instance, when the tube contains an explosive mixture of gases (which sometimes happens when phosphorus and hydriodic acid are used) or when it is desired to collect the gaseous products, the end of the capillary is carefully broken off with pincers or tongs—in the latter case inside a piece of pressure tubing connected with a suitable gas receiver.

After the capillary is opened, the tube is removed from the iron case, and the conical end broken off in the following manner. A deep file mark is made round the tube about 1 cm. below the shoulder, and the scratch is touched with the pointed end of a drawn-out glass rod which has been previously heated to redness in a blowpipe flame. In the majority of cases a crack forms at the file mark, and this may be led round the tube by touching the glass immediately in front of the crack with the heated point of the glass rod. If the thick end of a glass rod is used in these operations, the crack may form longitudinally on the tube. A piece of wire, bent to the shape of the tube and heated to redness, may be employed in place of the heated glass rod.

Another method which is not so liable to cause splintering at the cut is the following. The file mark is made as before. Two pieces of wet filter paper are rolled round the tube, one on each side of the file mark and about 0·5 cm. apart. The space between the papers is then heated by gradually bringing it into a pointed blowpipe flame, the tube being rotated the while. If the tube does not crack at once, it is given a few turns in the flame, after which the heated portion is moistened with a few drops of water, when the breaking off follows with certainty. In analytical work great care should be taken in opening as it is important to avoid the mixing of fragments of glass with the contents of the tube. The tube is then emptied of its contents.

(*b*) **Autoclaves.**—These are closed vessels made of iron, bronze or copper. Those in common use are made from cast steel, and hence are capable of standing great pressure. Such vessels are not suited for heating mixtures of a resultant acid reaction, but may be used for mixtures which are of neutral or alkaline reaction. When acidic substances are being dealt with, autoclaves covered on the interior with a resistant enamel are used, but unfortunately few enamels are very durable and in consequence the vessel has to be re-enamelled at intervals. Of the special alloys which are used for autoclaves, those containing 1—3% of Ni which are highly resistant to alkalis, and those containing 12% Si and 4—6% Al (Tantiron) which are practically unattacked by acids, are the most important. Fig. 41 represents a form of autoclave which is commonly used for experimental purposes. The body B of the autoclave is immersed in an oil or

metal bath. Along the flange of the body there runs a circular groove of rectangular section which is filled with lead (molten lead run in and allowed to solidify). On the lower surface of the flange of the lid there is a projecting ring which fits neatly into the lead-filled groove, and when the screws between the body and lid are tightened, a pressure-tight joint is formed at the lead ring. In order to secure a proper joint, judicious tightening of the screws (these should run easily at first) is necessary. To begin with, one nut is screwed home with the hand, the nut diametrically opposite is similarly treated, these are then alternately given a few turns with a wrench until they are moderately tight. The intervening nuts are then screwed home, each one a little at a time so as to maintain as far as possible a uniform pressure over the whole surface of the lead ring. This done, a further tightening—which may be repeated a few times—is given to all the nuts, going round them in circular fashion. During the heating, the nuts should be tested from time to time, and tightened if necessary. The lid of the autoclave is provided with two openings—one for a thermometer tube, and another for a pressure gauge, each of which is fixed by a screw pressure-tight joint; sometimes there is a third opening for a safety valve, but with a tested autoclave bought from a reliable firm a safety valve is unnecessary, and often an encumbrance. Such autoclaves should, however, be frequently tested by engineers. A tube may be provided with suitable valve for releasing the internal pressure when required. If such a tube dips into the liquid in the autoclave, samples can be withdrawn by carefully opening the valve while the autoclave is under pressure. Autoclaves may be emptied after completion of a reaction by a similar arrangement, when the pressure has fallen to, say, 4 or 5 atmospheres.

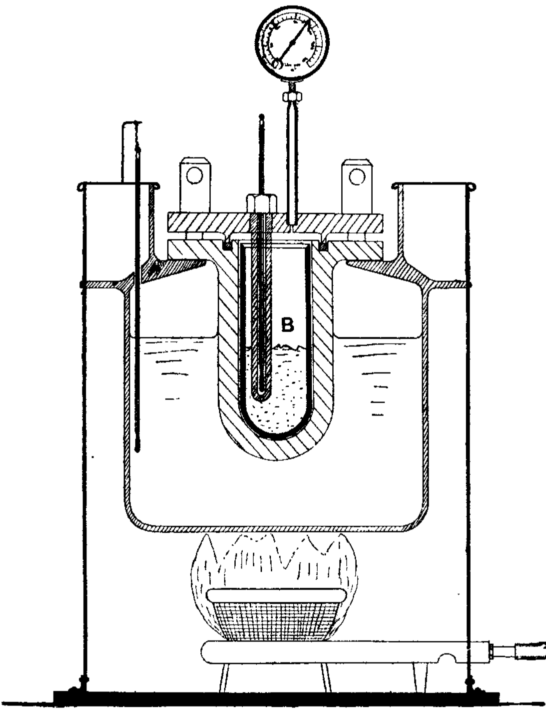



FIG. 41.

It is often convenient to place inside the body of an autoclave a neat

fitting pot of lead or enamelled metal. The space between the two vessels may be filled with molten solder or molten lead, but in many cases no such filling is used. The inner vessel serves to protect the main body of the apparatus, and its easy removability (when no filling is used)—on the small experimental scale at any rate—can be utilised in the charging and the emptying of the apparatus. The inner pot may be made of good enamelled iron to withstand acids, or Monel metal (67% Ni, 28% Cu, and 5% other metals) to withstand alkalis. During the operation of heating, oil or mercury sufficient to cover the bulb of a thermometer is placed in the thermometer tube. Autoclaves are made in various sizes with capacities ranging from half a litre up to a few thousand litres. Those which are provided with stirring gear are, of course, the more efficient, and details of these may be obtained from the catalogues of well-known manufacturers. The limits of temperature and pressure are about 500° C. and 200 atmospheres, and the greatest charge should not be more than about 75% of the volume of the vessel. Temperature of the outer bath, in which a thermometer is kept immersed, should be about 30° higher than the internal temperature. The screws must not be loosened so long as there is any pressure indicated on the gauge. When a charge contains ammonia or develops ammonia on heating, a manometer or gauge fitted with an iron and not with a bronze tube must be used, since ammonia vapours rapidly destroy copper or bronze tubes (J. S. C. I., 50 (C. and I.), 104).

## Density of Liquids

The density of a liquid is most easily determined by means of vessels known as pyknometers, the volume of which need not exceed 1 c.c. Perkin's modification (Fig. 42) of the Sprengel pyknometer is well adapted for small quantities of liquid and also for volatile liquids. The apparatus which usually has a volume of 2—10 c.cs. consists of a U-tube, the limbs of which are drawn out to capillaries, and bent as shown. On limb A a small bulb is blown, and below this a ring is etched round the capillary. The ends of the capillaries are fitted with loose glass caps.

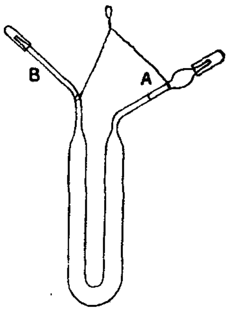


Fig. 42.

The apparatus is cleaned and dried by washing successively with water, alcohol, and ether, and then drawing air through the tube. The apparatus is first weighed empty, being suspended from the beam of a balance by a piece of platinum wire. Liquid is then drawn into the vessel through B until the bulb on A is half full. The apparatus is immersed in a bath at constant temperature—ice and water serve for 0°, while a thermostat should be used for higher temperatures. After standing in the bath for some time, the apparatus is inclined until limb B assumes a horizontal

position; a piece of filter paper applied to the end of this limb is allowed to absorb liquid until the meniscus on limb B sinks to the etched mark. The apparatus is then returned to a vertical position, the glass caps are replaced on the limbs, and after removing from the bath the whole is carefully dried with a good cloth and weighed. Afterwards the apparatus is cleaned and dried, and the operation repeated, using distilled water.

If both operations are carried out at the same temperature—

The approximate density $= \dfrac{W}{W_1}$

where $W$ = weight of liquid,
and $W_1$ = weight of water.

The absolute density $\left(D_4^t\right) = \dfrac{W}{W_1} \times D$,

where $D$ = density of water at 4°,
and $t$ = temperature of operations.

## The Polarimeter

The polarimeter is used for determining the specific rotations of optically active substances and also for determining concentrations of solutions of optically active substances of known specific rotation.

The polarimeter consists of two Nicol prisms N and $N_1$ (Fig. 43) set at a distance from one another and on a common axis. $N_1$ is the polariser and N the analyser. The polarimeter tube T, containing a definite length—usually 10 or 20 cms.—of liquid is placed between the two Nicols. Monochromatic light must be used, generally that from a sodium flame or from a mercury vapour lamp being employed. The light from F when using a sodium flame passes first through a bichromate cell C in order to give the pure sodium D light, then through a lens to the polariser; when using a mercury arc, the light is passed through a filter so as to give the green line (546·1$\mu\mu$). The K.B.B. Atmospheric Burner (p. 50) fitted with a hood and filter is a suitable means of supplying mercury vapour light. In the Laurent polarimeter a thin quartz plate P is inserted to cover half the field. In the Lippich type a small Nicol prism or two Nicol prisms are used instead of a quartz plate to cover part of the field; and this instrument possesses the advantage that it can be used with light of any wave length.

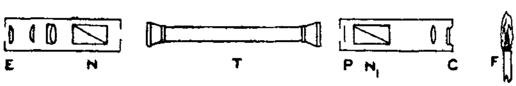


FIG. 43.

Light vibrating in only one plane passes through the polarimeter tube to the analyser N, which can be rotated about the main axis. The eye-piece at E consists of a system of lenses for focussing.

The flame produced from common salt or a sodium lamp is adjusted to give a maximum of light, the tube T being removed for the time being.

The polariser $N_1$ is fixed in position. The illuminated split disc is then focussed from the eyepiece E, and the analyser rotated until the whole field is of uniform intensity. The reading as indicated on a circular disc fitted with a vernier attached to the eyepiece is taken as the zero reading. This reading should be determined before every experiment. The substance of which the specific rotation is to be determined is placed in a clean dry polarimeter tube in the form of liquid or of solution so as to completely fill the tube. The tube is then placed in position in the polarimeter; the analyser is again turned until the intensity of illumination on each half of the disc is equal. The angle is again read on the scale, and this reading, minus the zero reading, gives the angle of rotation, $\alpha_D$. The temperature at which the observation is made should be noted; in some cases a jacketed polarimeter tube, through which water at a definite temperature is circulated, is used. The specific rotation—$\left[\alpha\right]_D^t$—at temperature $t$ of a pure liquid is calculated from the formula :—

$$\left[\alpha\right]_D^t = \frac{\alpha}{ld}$$

$\alpha$ = angle of rotation for sodium D line.
$l$ = length in decimetres of liquid in polarimeter tube.
$d$ = density of liquid at $t°$.

The specific rotation of an optically active compound in a pure solvent may be calculated from the formula :—

$$\left[\alpha\right]_D^t = \frac{100\alpha}{l\,c} \text{ or } \frac{100\alpha}{l\,d\,p}.$$

$c$ = gms. of active compound in 100 c.cs. of solution.
$p$ = percentage of solute by weight.

If the substance turns the plane of polarisation to the right, *i.e.*, clock. wise, it is said to be dextro-rotatory, and if to the left, lævo-rotatory- (See Findlay, " Practical Physical Chemistry.")

**Apparatus for certain Catalytic Preparations**

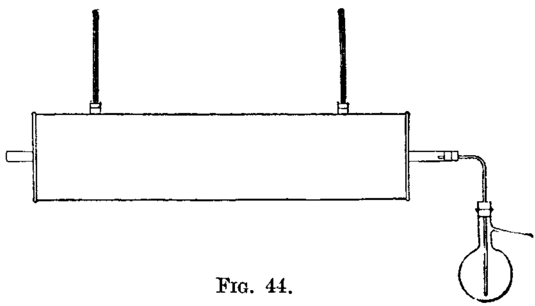


FIG. 44.

The following apparatus (Fig. 44) serves for such a large number of catalytic preparations that it may be considered general apparatus (see acetaldehyde, acetone and hexahydrophenol). The catalyst, generally distributed over some bulky material (*e.g.*, pumice, etc.) is placed in a combustion tube which is inserted through two holes in the ends of a long cylindrical air bath made of tin or light sheet iron. The air bath is of

such a length (about 75 cms.) that it fits on an ordinary combustion furnace by which it is heated ; its diameter is usually about 20 cms., and there are two openings in the top for the insertion of thermometers. Nitrogen-filled thermometers or thermo-couples are necessary for temperatures of 400° and above.

When a liquid is used in the reaction it may be led into the tube in the following ways, the method selected depending on the requirements of the reaction :—

1. A distilling flask is attached to the inlet end of the tube and the liquid distilled over, or it may be evaporated over in a current of gas.

2. A silica distilling flask surrounded by an air bath (a tin or iron box covered with a card of asbestos) is connected to the tube, the bath being heated to a high temperature, say 300°—400°. The liquid is dropped into the silica flask from a dropping funnel inserted through a cork in the neck of the flask ; by this means the rate of passage of vapours over the catalyst may be controlled, and further, the vapours are at a high temperature before coming into contact with the catalyst.

3. A bent dropping funnel is inserted through a cork in the inlet end of the combustion tube, the first 15 cms. of which is loosely packed with asbestos and is kept outside the air bath. The liquid is allowed to drop in slowly from the funnel. A small flame is lighted under the tube where the liquid drops, and the flames gradually increase in size as the catalyst is approached ; this precaution is to prevent breakage.

A solid, if easily volatile, may be treated as for a liquid. In some cases it may be steam distilled over the catalyst.

Most experiments of this kind require efficient apparatus for condensing the products of reaction ; owing to the high temperature it is generally advisable to pass these first through an empty flask and then through some efficient type of condenser. The condensing apparatus may be attached to the exit end of the combustion tube by means of a cork and delivery tube, or the exit end of the combustion tube may be bent and drawn out after the shape of an adapter.

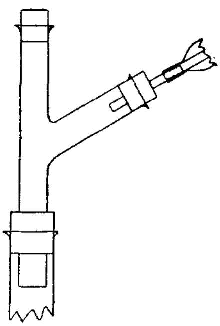


Fig. 45.

### Addition Tube

The Y-shaped tube (Fig. 45) is a most convenient apparatus through which to make additions to a mixture which is being heated under a reflux condenser. It is particularly useful for the addition of solids (for example, sodium—see p. 366). For the addition of liquids a dropping funnel is introduced through a cork in the upright limb.

**The K.B.B. Atmospheric Burner** (Kelvin, Bottomley and Baird).—This lamp (Fig. 46) is a very convenient source of ultra-violet and monochromatic illumination. The quartz tube, which is not evacuated, is incompletely filled with air-free mercury. The current passes from the + electrode A to the − electrode B through the mercury,

a small heating unit E being incorporated in the circuit. When the current is passed, this latter heats the mercury in the narrow tube at E to boiling, the mercury vapour thus formed displacing the mercury into the reservoir. An arc is then struck through the mercury vapour. A device is fixed which cuts out the heating unit when the pressure of mercury vapour

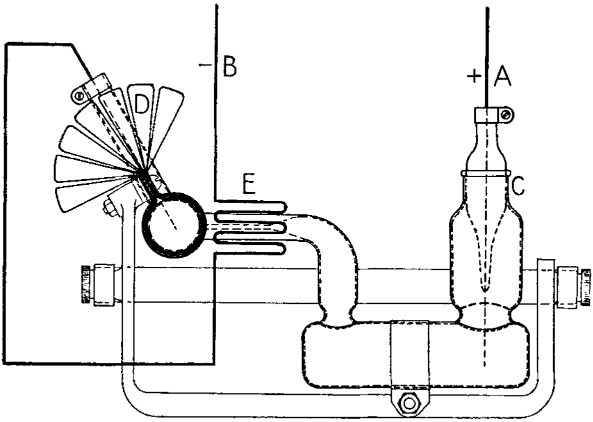



Fig. 46.

increases to a certain level. The — electrode is kept from becoming too hot by the aluminium cooling fins D. When the lamp deteriorates, the glass stopper at C is removed and the mercury poured out and cleaned. If the quartz becomes discoloured, it can be heated in a blowpipe flame. (See Prep. 346 and Reactions LXXIV. (*b*) and CLXVIII.)

**Chromatographic Analysis.**—Chromatographic adsorption-analysis, the most delicate method of separation of closely related compounds, depends on the simultaneous adsorption and separation of mixtures of organic compounds, such as natural dyes, biochemical products, isomerides, hydrocarbons, etc., in suitable solvents such as petroleum, ether, chloroform, carbon disulphide and water.

The solution is dropped through a glass column containing the adsorbent alumina (aluminiumoxid nach Brockmann, Merck), Fuller's earth, calcium hydroxide, calcium carbonate or magnesia. The rate of adsorption of the components of the solution varies and the separated components, which occur in various layers of the adsorbent, may then be removed by washing with a suitable solvent or mixture of solvents. The tube containing the adsorbent is evenly packed by adding it in the form of a cream made up with solvent, the latter being removed under slight vacuum. The column is kept covered by solvent throughout the analysis, and the solution to be examined is drawn through the adsorber by means of a siphon. This is followed by a solvent, not necessarily the original, until the different zones in the column are separated. The main advantage of the process is that all material can be recovered quantitatively, and a complete separation can be effected at room temperature, and, if necessary, in the absence of air. For further information and references, see J. S. C. I., 1936, 724.

# PART II

## CHAPTER III

### THE LINKING OF CARBON TO CARBON

### Hydrogen Compounds

In this section are described those preparations in which carbon atoms are caused to unite with one another. It is this property, whereby carbon atoms unite to form molecules of seemingly unlimited complexity, which has led to the study of the carbon compounds being made a special branch of chemistry, and these reactions are, theoretically at any rate, the most important of all those discussed.

**Reaction I. Passage of the Vapour of certain Hydrocarbons through a red-hot Tube** (A., 230, 5.)—A large number of hydrocarbons condense to form hydrocarbons of higher molecular weight when their vapour is passed through a red-hot tube. The method, however, is only of theoretical importance, for the yield is in most cases small owing to incomplete conversion, and to the formation of a large number of by-products. Benzene has been obtained from acetylene in this way; benzene itself, and diphenyl methane treated in a similar manner, give diphenyl and fluorene respectively.

$$\mathrm{R.H + H.R \xrightarrow{\text{Heat}} R.R + H_2,}$$

where R.H is a hydrocarbon.

Preparation 1.—**Diphenyl** (*Phenylbenzene*).

$$\mathrm{C_6H_5.C_6H_5. \qquad C_{12}H_{10}. \qquad 154.}$$

*Method I.*—In this experiment the apparatus shown in Fig. 47 is used. The flask, of about 1½ litres capacity, contains 500 gms. of benzene kept boiling by means of a water bath. The flask is provided with a cork having two perforations, through one of which the tube *a* passes while the second accommodates the tube *b*. This leads to the iron tube R (a wrought-iron gas pipe of 1 metre length, and 20 mms. internal diameter), which is filled with pieces of pumice, and heated by means of a combustion furnace or a Fletcher's gas furnace to a bright red heat. From the flask the benzene vapour passes into the glowing tube, and is here partially converted into diphenyl, hydrogen, and other products. The unchanged benzene and the volatile diphenyl pass through the tube *e* into the condenser K and flow from it through *a* back into the flask. The tube *a* dips

below the level of the liquid, and at *d* has a tube sealed on for the escape of the hydrogen. The operation is carried on for from 6 to 10 hours, the apparatus acting automatically. The flask now contains a fairly concentrated solution of diphenyl in benzene. The latter is removed on a water bath, and the residue is fractionated. The part passing over above 150° solidifies in the receiver, and consists of almost pure diphenyl. It may be purified by crystallisation from alcohol. The yield is greatly dependent on the temperature of the iron tube. With a low gas pressure the ordinary combustion furnace is almost useless ; in that case it is better to substitute a Fletcher's gas furnace or a charcoal furnace for it.

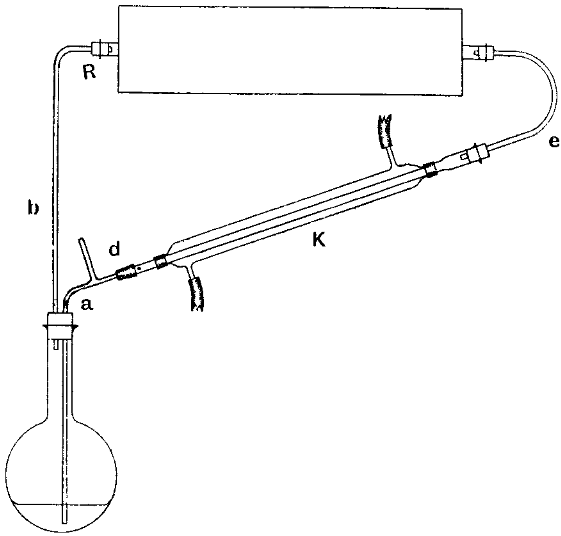



FIG. 47.

$$2C_6H_6 = C_6H_5.C_6H_5 + H_2.$$

*Yield.*—Up to 20% theoretical (100 gms.). $D._4^{82}$ 0·9845. (Z. Ch., 1866, 707 ; A., 230, 5 ; U.S.P., 1894283 ; E.P., 369613.)

This " thermal condensation " can also be brought about by exposing the vapour of benzene to the action of a wire or filament kept at red heat by an electric current.

*Method II.*—The apparatus is as follows :—Two copper wires pass tight-fitting through the cork in the neck of a flask, and are connected together above the benzene in the flask by a coiled platinum wire, 25 cms. long and 0·2 mm. in diameter. A reflux condenser is fitted to the side tube of the flask. 50 gms. of benzene are boiled on a water bath in the flask. After fifteen minutes' boiling the air in the flask will have been expelled, and the current is switched on and regulated by means of a variable resistance so that the platinum spiral glows red (4—4·5 amps. ; 8—10 volts). A battery of accumulators can be used as a source of current, or the latter can be obtained from an alternating service supply at 110 or 220 volts, the necessary reduction in current and voltage being brought about by a rheostat or a bank of lamps. In the latter case it is more economical to use the thread of a carbon lamp instead of a platinum wire. After 5 hours a portion of the benzene will have been converted into diphenyl under the action of red heat. The unaltered benzene is removed

on a water bath, and the residual liquid fractionated from a small flask, the portion 240°—270° being collected separately, and recrystallised from alcohol or from a mixture of benzene and petroleum ether—

$$2C_6H_6 = C_6H_5.C_6H_5 + 2H.$$

*Yield.*—22% theoretical (11 gms.). Colourless leaflets; soluble in benzene; M.P. 71°; B.P. 254°; D. $^{82}_{4}$ 0·9845. (Z. e., 7, 903.)

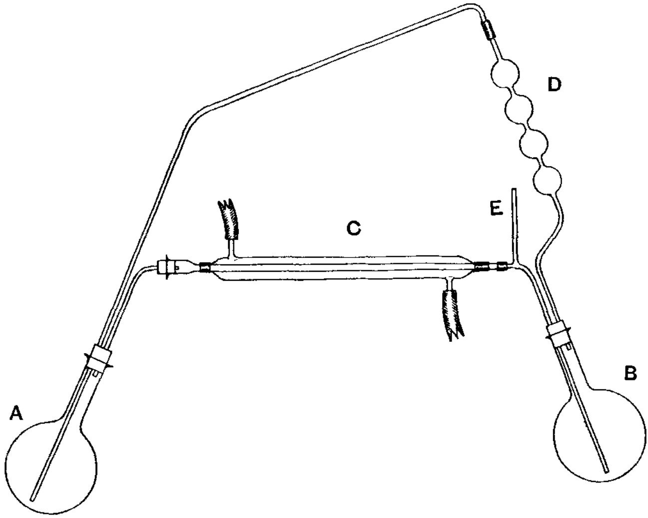



FIG. 48.

**Reaction II. Reduction under certain Conditions of Aromatic Ketones.** (A., 194, 310.)—When aromatic ketones are reduced by zinc dust in the presence of glacial acetic acid pinacones are formed (see p. 70).

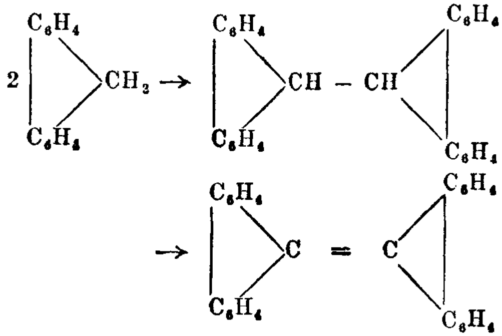
$$2C_6H_5.CO.C_6H_5 + 2H = (C_6H_5)_2C.(OH).C(OH).(C_6H_5)_2.$$

If hydrochloric acid is added the reduction goes to the corresponding hydrocarbon; *e.g.*, from benzophenone *s*-tetraphenylethane is obtained.

$$2C_6H_5.CO.C_6H_5 + 6H \longrightarrow (C_6H_5)_2.CH.CH.(C_6H_5)_2.$$

**Reaction III. Oxidation under certain Conditions of Lower Hydrocarbons.** (B., 32, 432.)—In this reaction two molecules of a hydrocarbon are condensed, hydrogen being eliminated by the action of an oxidising agent. Two neutral oxidising agents, potassium persulphate and lead oxide, are especially useful in this type of reaction. The former is used in dilute aqueous solution, at a temperature of about 100°; to obtain results with the latter much higher temperatures are necessary. The substance is mixed with the lead oxide and heated to over 250°, or it is distilled over heated lead oxide. The results obtained vary with the temperature and the amount of lead oxide used, *e.g.*, fluorene can be oxidised to either

bidiphenylene-ethane or bidiphenylene-ethylene. With potassium persulphate the first stage only is reached.



It is to be noted that to obtain practicable yields this reaction must be confined to aromatic hydrocarbons. In the aliphatic series it only takes place, in a few cases, and then gives but a yield of the order of 1%.

PREPARATION 2.—*s*-**Diphenylethane** (*Dibenzyl*).

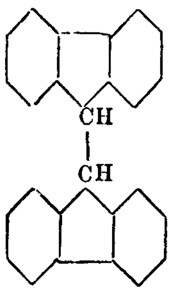
$C_6H_5CH_2.CH_2.C_6H_5$. $C_{14}H_{14}$. 182.

90 gms. potassium persulphate (1 mol.) are dissolved in a litre of water, and to this is added 60 gms. (2 mols.) of toluene. The mixture is heated on a water bath for 4 hours in a flask fitted with good agitation and a reflux condenser (see Fig. 38). The oily layer is then separated, dried over calcium chloride and fractionally distilled, the fraction 270°—280° consisting of dibenzyl and benzoic acid being separately collected. The earlier fractions consist of toluene and benzaldehyde. The dibenzyl fraction is dissolved in ether and the benzoic acid removed by shaking with dilute caustic soda solution. The ether is then removed on the water bath, and the residue recrystallised from dilute alcohol.

$$4C_6H_5.CH_3 + O_2 \rightarrow 2C_6H_5CH_2CH_2C_6H_5 + 2H_2O.$$

*Yield.*—15% theoretical (9 gms.). Colourless monoclinic needles; M.P. 51°—52°; B.P. 284°; $D._{50}^{50}$ 0·9752. (B., 32, 432, 2531.)

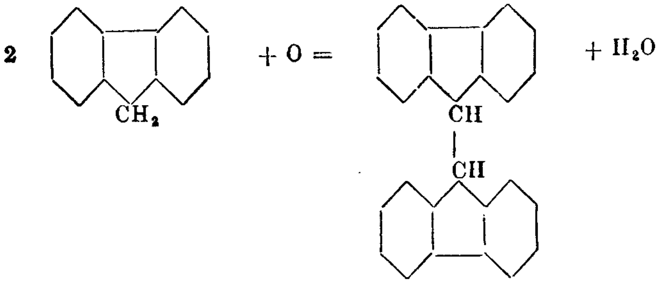
PREPARATION 3.—**Dibiphenylene-ethane.**



$C_{26}H_{18}$. 330.

10 gms. (2 mols.) of fluorene, and 15 gms. (excess) of lead oxide are thoroughly mixed and heated with slow stirring in a metal crucible in a

bath till the temperature of the latter reaches 270°, where it is kept for 2 hours. The crucible is cooled to 150°, wiped clean, and plunged into cold water. The contents, which are by this means loosened, are ground up, extracted with boiling benzene, and the extract concentrated to small bulk. The crystals which separate are recrystallised from benzene, or glacial acetic acid. The mother liquors contain unaltered fluorene.




*Yield.*—50% theoretical (5 gms.). Colourless crystals; slightly soluble in alcohol and ether; soluble in hot benzene and glacial acetic acid; M.P. 246°. (A., 291, 6.)

**Reaction IV.** (*a*) **Action of Dehydrating Agents on a Mixture of an Aromatic Hydrocarbon and an Aromatic Alcohol.** (B., 6, 964.)—This reaction, which was discovered by Baeyer, gains importance from its similarity to the methods used in preparing such substances as phenolphthalein and fluorescein (see pp. 107, 385).

Various dehydrating agents—concentrated sulphuric acid, zinc chloride, phosphorus pentoxide—can be used. Sulphuric acid, although perhaps the most convenient, has the disadvantage that it tends to sulphonate the aromatic substances employed. At a low temperature, however, diphenylmethane can be obtained from benzyl alcohol and benzene. At 140° phosphorus pentoxide condenses benzene and diphenylcarbinol to triphenylmethane (see B., 7, 1204). Not only substituted benzyl alcohols, but even mandelic acid can be brought within the scope of the reaction, while in place of benzene its nitro, amino or phenolic derivatives may be used.

$$RR_1CH\,\boxed{OH + H}\,R_{11} = RR_1CHR_{11} + H_2O.$$

Preparation 4.—**Diphenylmethane** (*Benzylbenzene*).

$CH_2.(C_6H_5)_2$. $C_{13}H_{12}$. 168.

A mixture of equal weights of concentrated sulphuric acid and glacial acetic acid is run into a mixture of 10 gms. (1 mol.) of benzyl alcohol, 27 gms. (excess) of benzene and 100 gms. of glacial acetic acid until most of the benzene has separated on the surface. After 12 hours, 500 gms. of concentrated sulphuric acid are added under constant cooling, and the mixture again allowed to stand for 6 hours. The mass is then poured into water, extracted with ether, the extract dried over calcium chloride, and

the residue, after removing the ether on a water bath, fractionated under reduced pressure, the fraction 174°—176° at 30 mms. being separately collected.

$$C_6H_5.CH_2OH + C_6H_6 = C_6H_5.CH_2.C_6H_5 + H_2O.$$

*Yield.*—25% theoretical (4 gms.). Colourless oil; on cooling solidifies to needle-shaped crystals; orange-like odour; M.P. 26°; B.P. $^{760}$ 263°; B.P. $^{30}$ 175°; D. $^{25}_{25}$ 1·0056. (B., 6, 964.)

**Reaction IV.** (*b*) **Action of Dehydrating Agents on certain Ketones.** (J. pr., 15, 129.)—This is a reaction of historical interest, for it was by the preparation from acetone by distillation with fairly strong sulphuric acid that the symmetry of mesitylene was deduced, and hence the orientation of such compounds as *m*-xylene was established.

Besides its dehydrating action, the purely condensing capabilities of sulphuric acid should not be overlooked. Thus methyl acetylene condenses in the presence of sulphuric acid to mesitylene. (B., 29, 958, 2884.)

$$3CH_3C \vdots CH = C_6H_3(CH_3)_3.$$

This reaction is similar to the polymerisation of acetylene to benzene by the action of heat.

PREPARATION 5.—**Mesitylene** (s-*Trimethylbenzene*).

$$C_6H_3(CH_3)_3[1:3:5]. \qquad C_9H_{12} \qquad 120.$$

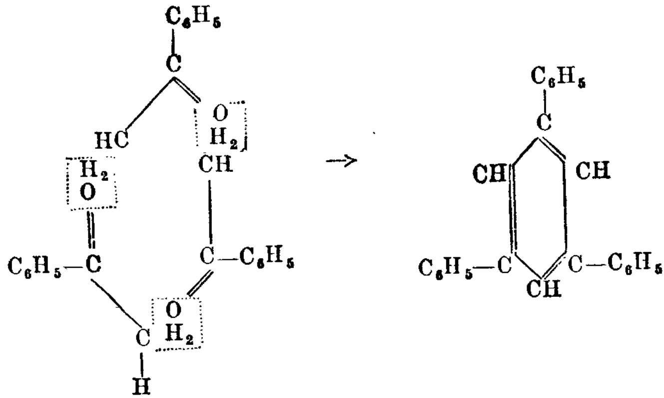
400 gms. of clean dry sand are placed in a 2-litre retort connected with a condenser. 250 gms. (3 mols.) of acetone are added, and then a cooled mixture of 560 gms. of concentrated sulphuric acid and 150 gms. of water is run in, in a *slow* continuous stream, the retort being meantime cooled in cold water. After 24 hours' standing, the mixture is slowly distilled, directly or in steam. When oily drops appear in the neck of the retort, the receiver is changed, and the distillate collected until only very small quantities of the oil appear. The colour of the liquid (if directly distilled) changes to deep brown, and finally to black, sulphur dioxide is evolved, and the mass froths up considerably. The upper yellowish layer of the distillate is separated from the lower aqueous layer, washed with caustic soda and water, and dehydrated over calcium chloride. It is then fractionated, the fraction 100°—200° being redistilled four times over thin slices of metallic sodium, when about two-thirds of it is obtained as pure mesitylene coming over at 161°—166°.

$$3CH_3.CO.CH_3 = C_6H_3(CH_3)_3 + 3H_2O.$$

*Yield.*—Variable, about 25% theoretical (40 gms.). Colourless, strongly refracting liquid; B.P. $^{760}$ 163°; D. $^{10}_{4}$ 0·8694. (J. pr., 15, 129; A., 147, 143; 278, 260; Bl., 40, 267; Am. Soc., 15, 256; 20, 807; O.S., II., 41.)

Acetophenone condenses in a similar manner if it is heated with phosphorus pentoxide, or better if saturated with dry hydrogen chloride at ordinary temperatures. *s*-Triphenylbenzene is deposited after standing

for several days in a warm place; by resaturating the mother liquors, yields up to 50% can be obtained.



**Reaction V. Cinnamic Condensation and Elimination of Carbon Dioxide.** (Am. Soc., 1, 313.)—This is an extension of Perkin's reaction, and depends on the fact that when benzaldehyde and phenyl-acetic acid are condensed in the usual way, the unsaturated acid thus formed is unstable, and loses carbon dioxide, giving stilbene.

$$C_6H_5.CHO + H_2C.(C_6H_5)COOH \longrightarrow$$
$$C_6H_5CH : C(C_6H)_5COOH \longrightarrow C_6H_5CH : CH.C_6H_5.$$

Technically this method is of no importance, as the hydrocarbon is obtained from coal-tar.

**Reaction VI.** (*a*) **Action of certain Anhydrous Metallic Halides on a Mixture of an Aromatic Hydrocarbon and an Alkyl Halide.** (Friedel-Crafts.) (C. r., 1877, 1450.)—The "Friedel-Crafts" reaction, of which the above illustrates one phase, is one of the most important condensing reactions known to organic chemistry. Applied to the production of aromatic hydrocarbons and their derivatives, the action consists in the catalytic use of anhydrous aluminium chloride for condensing an aromatic hydrocarbon or its derivatives with a chloro- or bromo-compound. Halogen acid is always evolved, and the product is a compound with aluminium chloride which decomposes, yielding the required compound on addition of water. Not only does the reaction proceed without the use of heat in most cases, but frequently it must be moderated by using a large excess of the hydrocarbon, or better by diluting with some neutral solvent, such as ligroin, carbon disulphide, or nitrobenzene. The two former diluents automatically keep down the temperature to their boiling points; the latter has the especially useful property of dissolving anhydrous aluminium chloride. If a hydrocarbon derivative is used, coupling takes place in the *para* position or, if that is occupied, in the *ortho*, but the yield suffers. In place of aluminium chloride, aluminium bromide (D.R.P., 126421), aluminium foil and hydrogen chloride (B., 28, 1136), mercuric

chloride (see Reaction VI. (*b*) ), ferric chloride, zinc chloride (B., 30, 1766), the aluminium-mercury couple (Reaction VI. (*c*) ) can be used in some cases. (See also C. r., 84, 1392 ; B., 18, 2402 ; 33, 815. For other uses of this reaction, see pp. 85, 121.)

The methods employed vary but little. The aluminium chloride is slowly added to a mixture of the hydrocarbon and the alkyl halide, or the alkyl halide is added to a mixture of the other two. The latter process is mostly used with volatile halides which are led in gaseous form into the mixture of the other two components, for a time which varies as the number of alkyl groups it is desired to introduce.

$$RCl + AlCl_3 = RClAlCl_3$$
$$RClAlCl_3 + R_1H = RR_1AlCl_3 + HCl$$
$$RR_1AlCl_3 + H_2O = RR_1 + AlCl_3 + H_2O.$$

*Note.*—Bottles filled with aluminium chloride have frequently a high internal pressure and must, therefore, be opened with great care, being covered with a cloth during this operation.

For some anomalies in the behaviour of aluminium chloride as compared with that of aluminium bromide, see A., 225, 155.

PREPARATION 6.—**Triphenylmethane** (*Methenyltriphenyl*).

$$CH(C_6H_5)_3. \qquad C_{19}H_{16}. \qquad 244.$$

40 gms. (1 mol.) of chloroform which has stood for 12 hours over calcium chloride is mixed with 200 gms. (excess) of similarly treated benzene in a retort connected to an upright condenser. The operation is carried out in a fume cupboard. 30 gms. of anhydrous aluminium chloride (see p. 506) are added in 5-gm. lots every 5 minutes with constant shaking. The reaction is completed by boiling for half an hour on a water bath, the retort cooled, and its contents *very cautiously* poured into an equal volume of ice-cold water. The upper layer of triphenylmethane dissolved in benzene is separated, dried over calcium chloride, the benzene removed on a water bath, and the residue fractionated to 200°. It is then distilled under reduced pressure from a retort without a condenser. Impure triphenylmethane first distils and then the distillation slackens. The retort is more strongly heated till the distillate no longer solidifies on cooling. The crude triphenylmethane in the receiver is twice recrystallised from hot benzene, heated on a water bath to remove " benzene of crystallisation " and finally recrystallised from hot alcohol.

$$CHCl_3 + 3C_6H_6 = CH(C_6H_5)_3 + 3HCl.$$

*Yield.*—33% theoretical (25 gms.). Colourless rhombic plates; M.P. 92°; B.P. $^{760}$ 350°; D. $\frac{95}{95}$ 1·0568. The compound with benzene has the formula $C_{19}H_{16}.C_6H_6$.

*Note.*—The aluminium chloride used must be recently made and of good quality, otherwise it must be resublimed from a retort, as it is essential it should be anhydrous. (C. r., 1877, 1450; B., 26, 1961; Bl., 37, 6; A., 197, 252; O.S., IV., 81).

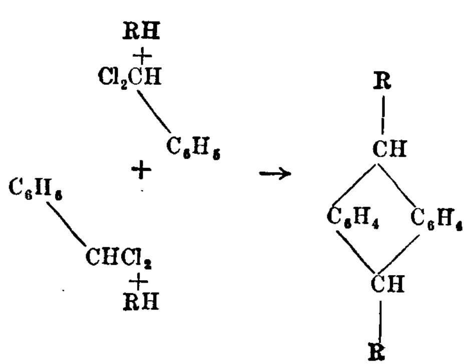
**Reaction VI.** (*b*) **Action of Aluminium and Mercuric Chloride on a Mixture of an Aromatic Hydrocarbon and an Alkyl Halide.** (J. C. S., 117, 1335.)—This is a development of the Friedel-Crafts reaction which has lately yielded some very interesting results. As far back as 1895 an attempt to use a mixture of aluminium powder and mercuric chloride in the ordinary Friedel-Crafts reaction ended in failure (B., 28, 1139). Later (B., 37, 1560), it was proved that mercuric chloride and aluminium in benzene or toluene formed compounds of the type $C_6H_6.AlCl_3.HgCl$. It was by the use of these double compounds that the secondary reactions, which caused the failure of the earlier attempts, were avoided and some very interesting condensations brought about. In the formation of the catalyst the following reaction occurs:

$$C_6H_6 + Al + 2HgCl_2 \longrightarrow C_6H_6.AlCl_2.HgCl + Hg.$$

An excess of mercuric chloride must be used to prevent the mercury liberated amalgamating with the aluminium, for the couple so formed would act concurrently with, but in a different manner to, the double compound (see the next reaction).

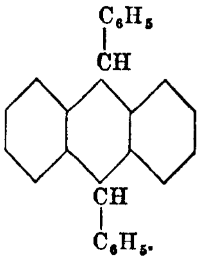
Applied to the synthesis of hydrocarbons the following results have been obtained by this new method. 9 : 10-Diphenyl-9 : 10-dihydroanthracene is formed by the condensation of benzene and chloroform, whilst in the ordinary Friedel-Crafts reaction (A., 194, 254; 227, 107) triphenylmethane (Preparation 6) is the main product, traces of chlorarylmethanes and tetraphenylethane (B., 26, 1952) being also formed. The same compound is also obtained from benzal chloride and benzene. Carbon tetrachloride and benzene give 9 : 9 : 10 : 10-tetraphenyl-9 : 10-dihydroanthracene as do also phenylchloroform and benzene. In the older reaction triphenylchloromethane (p. 432) is the chief product.

Chloroform and toluene yield by this process dimethyl-9 : 10-ditolyl-9 : 10-dihydroanthracene; using aluminium chloride, tetratolylethane is obtained (B., 14, 1530). Benzylidene chloride and toluene yield dimethyl-9 : 10-diphenyl-9 : 10-dihydroanthracene.




For other applications of this reaction see pp. 89, 121.

PREPARATION 7.—**9 : 10-Diphenyl-9 : 10-dihydroanthracene.**



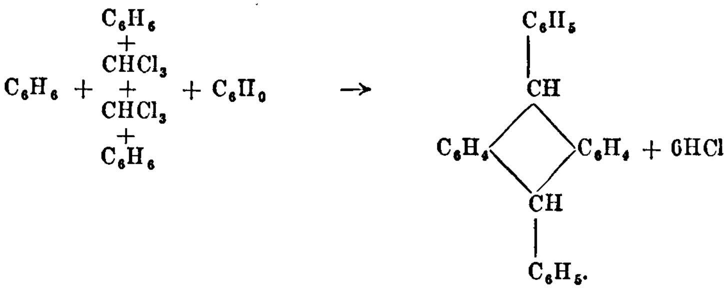
$C_{26}H_{20}$. 332.

**Preparation of Catalyst.**—13 gms. (excess) of dry benzene and 20 gms. (excess) of mercuric chloride are treated, gradually, in a flask fitted with a reflux condenser, with 1 gm. of aluminium powder, the flask being meanwhile vigorously shaken and occasionally cooled in ice-water. A green crystalline mass separates, and the reaction is completed by immersing the flask in tepid water for half an hour. The mercury liberated in the reaction is removed, and the catalyst is then ready for use.

9 gms. (2 mols.) of chloroform are added drop by drop through the condenser, and the flask left at ordinary temperature for 2 hours, heated for an hour at 40° and then for an hour at 40°—50°. During the whole course of the reaction the contents of the flask are well agitated by a mechanical stirrer (see the apparatus shown on p. 41).

On cooling, the product is decomposed with ice and filtered. From the filtrate a deep-red oil separates, from which all unchanged benzene is evaporated, and the residue extracted with boiling acetic acid containing a little water. The compound which separates on cooling is recrystallised from dilute alcohol, and then repeatedly from acetone.

The same compound can be prepared from 8 gms. (2 mols.) of benzal chloride, 13 gms. (excess) of benzene, and the above quantities of aluminium and mercuric chloride. The reaction is completed at 50°—55°. Otherwise the details are as already described.




Colourless crystals: soluble in alcohol; M.P. 159° (J. C. S., *loc. cit.*); M.P. 164·2° (Am. Soc., 13, 556). Oxidised with chromium trioxide in glacial acetic acid solution, yields anthraquinone; gives a diacetyl derivative on heating with acetic anhydride and pyridine (J. C. S., 117, 1335).

**Reaction VI.** (*c*) **Action of the Aluminium-Mercury Couple, or of certain finely divided Metals on a Mixture of an Aromatic Hydrocarbon and an Alkyl Halide.** (J. C. S., 67, 826.)—The action of the couple is analogous to that of anhydrous aluminium chloride. Zinc dust or finely divided copper can also be used.

PREPARATION 8.—**Diphenylmethane** (*Benzylbenzene*).

$C_6H_5.CH_2.C_6H_5.$ $C_{13}H_{12}.$ 168.

1 gm. freshly prepared aluminium-mercury couple (p. 181) is added to 65 gms. (excess) of *dry* benzene in a flask attached to an upright condenser, the whole being placed in a fume cupboard. 32 gms. (1 mol.) of benzyl chloride are slowly dropped in from a tap funnel, during an hour, through the top of the condenser. The flask is then heated on a water bath for 15 minutes, its contents shaken with a very dilute solution of caustic soda, and the benzene solution separated. The aqueous portion is again extracted with benzene, and the whole benzene solution dehydrated over calcium chloride, the benzene removed on a water bath, and the residue distilled under reduced pressure, the fraction, 174°—176° at 80 mms., being retained.

$$C_6H_5CH_2Cl + C_6H_6 + (Al/Hg) = C_6H_5.CH_2.C_6H_5 + HCl + (Al/Hg).$$

*Yield.*—33% theoretical (14 gms.). Properties (see p. 56). (J. C. S., 67, 826; O.S., XIV., 34.)

**Reaction VI.** (*d*) **Ethylation of Benzene and Naphthalene by means of Ethylene in presence of Anhydrous Aluminium Chloride.**—Ethyl chloride in presence of aluminium chloride reacts with benzene to give ethyl- and poly-ethyl-derivatives of benzene (Reaction VI. (*a*) ). Ethylene and hydrogen chloride may be used in place of ethyl chloride, but as hydrogen chloride is evolved in the reaction little of this is necessary (Bl., 31 (2), 539). Ethylene and aluminium chloride will also react, the latter probably containing traces of water, etc., sufficient to supply the hydrogen chloride to maintain the reaction. By this method good yields of ethyl benzene can be obtained, while naphthalene can be ethylated in presence of benzene, the alkyl group being transferred from the latter to naphthalene in presence of aluminium chloride. Higher alkylated derivatives are also formed in each case. High speed agitation is essential (Am. Soc., 44, 206).

PREPARATION 9.—**Ethyl Benzene.**

$C_2H_5.C_6H_5.$ $C_8H_{10}.$ 106.

*Ethylene.*—The apparatus consists of an ordinary combustion tube packed with bauxite which has been previously ignited to 850° and sifted through a 400 mesh sieve. The tube is placed in an electric furnace (p. 448) and maintained at 350°. To one end of this tube is attached by the side tube a small distilling flask heated on a metal bath at 95°—105°, while a dropping funnel of sufficient length to overcome back pressure is also fixed to the flask for the addition of alcohol. At the other end of the tube is attached a sloping condenser leading to a distilling flask, the

side tube of which leads to a wash-bottle containing conc. sulphuric acid. The wash-bottle is connected to the reaction flask (Fig. 49) fitted with very efficient agitation, and heated on a water bath.

Absolute alcohol is placed in the funnel and the tap arranged so as to deliver 36 c.cs. per hour. This is vaporised on dropping into the hot flask, and passes into contact with the bauxite. 50 gms. of ethylene are produced in 3 hours, any unchanged alcohol being condensed in the distilling flask.

*Ethyl Benzene.*—116 gms. of pure benzene are placed in the reaction flask and stirred at about 1,500 revs. per minute, the temperature being maintained at 75°—80°. The reaction is stopped in 3 hours, when on standing the reaction product separates into two layers, the upper almost colourless, the lower brown and viscous. The latter is discarded. The upper layer is washed with dilute hydrochloric acid, then with water, and dried with calcium chloride. It is then fractionated, the fractions 80°—100°, and 100°—150°, being collected (p. 22). These are then finally fractionated and the fraction 134°—136° collected.

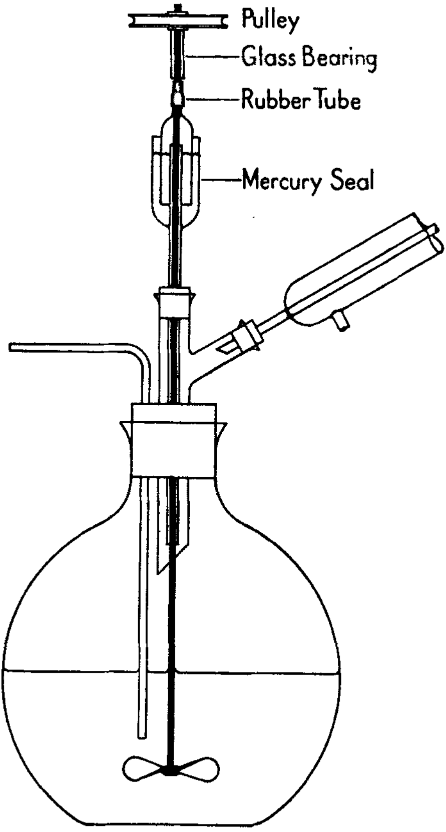


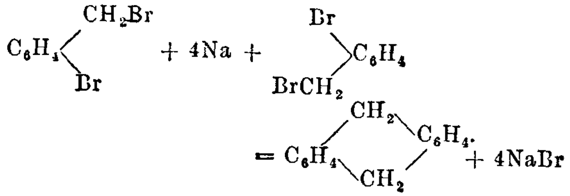

FIG. 49.

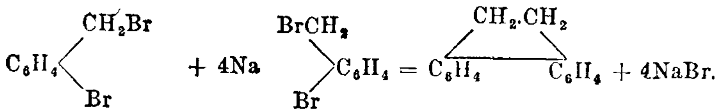
*Yield.*—50% theoretical (74 gms.). Colourless liquid; B.P. 134°; D. 0·866. (Z. a., 41, 955.)

**Reaction VII.** (*a*) **Action of Sodium on Halogen Compounds** (Würtz, Fittig, and Freund). (A., 131, 303.)—The application of this reaction to the synthesis of paraffins by Würtz was of great importance to chemical theory, as it afforded strong evidence of the chain linking of carbon atoms, and enabled the structure of many hydrocarbons to be determined by their syntheses.

Fittig applied the reaction to aromatic hydrocarbons. In this latter case a second side-chain may be introduced from a di-halogen derivative, simultaneously with the first or subsequently in a second reaction. All the possibilities of the reaction are illustrated in the synthesis of anthra-

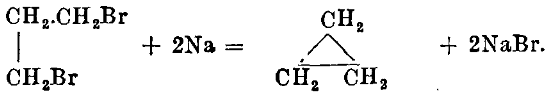
cene hydride and phenanthrenehydride simultaneously from *o*-bromobenzyl bromide. (B., 12, 1965.)





The reaction does not occur with the same readiness in all cases, the yields obtained varying greatly. In general, a basic group *para* to the halogen, and an acidic group *ortho* to the halogen, favour condensation. If the reaction is sluggish, it may be promoted in many cases by raising the temperature or by adding a little ethyl acetate (J. C. S., 67, 656). If the reaction is too vigorous, an indifferent solvent, *e.g.*, toluene, ether, or ligroin, is added to moderate it. Since the discovery of the Friedel-Crafts reaction, its very wide and varied application has led to its supplanting the Fittig method, than which in most cases it gives better yields.

Freund applied the method to the synthesis of cycloparaffins. From trimethylenedibromide, trimethylene was prepared, whilst hexamethylenedibromide yielded hexamethylene in a similar manner. (M., 3, 626; A. Ch., [5], 14, 488.)



When nitro groups are present copper powder gives better results (Reaction VII. (*b*) ).

Preparation 10.—**Ethyl Benzene** (*Phenylethane*).

$$C_6H_5.C_2H_5. \qquad C_8H_{10}. \qquad 106.$$

30 gms. (excess) of metallic sodium in the form of small pieces of wire are slowly added to 120 c.cs. of anhydrous ether prepared from commercial ether as described on p. 216. The ether is contained in a round flask (1 litre) which when the evolution of hydrogen has ceased, is attached to an upright condenser and immersed in a vessel of ice-water. A mixture of 78 gms. (2 mols.) of bromobenzene and 70 gms. (excess) of ethyl bromide, both carefully dehydrated, is added, and the mixture left to stand overnight. The liquid is then decanted from the sodium bromide, which has a blue colour, and the latter washed twice with dry ether. The ether is removed on a water bath, and the residue fractionated from a small distilling flask, the fraction, 132°—135°, being collected separately.

$$C_6H_5Br + C_2H_5Br + 2Na = C_6H_5.C_2H_5 + 2NaBr.$$

*Yield.*—60% theoretical (30 gms.). Colourless liquid; B.P. 134°; D. $^{22.5}_{4}$ 0·8664. (A., 131, 303.)

*Note.*—The residue in the flask contains unaltered sodium. This must be destroyed by adding the residue in small portions to alcohol, and allowing to stand till all action ceases.

PREPARATION 11.—**Dibenzyl** (s-*Diphenylethane*).

$$C_6H_5.CH_2.CH_2.C_6H_5. \qquad C_{14}H_{14}. \qquad 182.$$

12 gms. (slightly more than 2 mols.) of sodium wire are added to 50 gms. (2 mols.) of benzyl chloride, the whole refluxed on a water bath until no further change takes place, extracted with dry ether, and the extract fractionated, the fraction 244°—254° being retained, and recrystallised from alcohol. The reaction goes best in the absence of a solvent, but toluene can be added to lower the refluxing temperature.

$$2C_6H_5CH_2Cl + 2Na = C_6H_5.CH_2.CH_2.C_6H_5 + 2NaCl.$$

Colourless needles; soluble in benzene and in hot alcohol; M.P. 51°—52°; B.P. 248°; D. $^{50}_{50}$ 0·9752. (A., 121, 250; 137, 258.)

**Reaction VII.** (*b*) **Action of Metals other than Sodium on Halogen Compounds.** (B., 34, 2176.)—In the aliphatic series the iodo compound is heated, usually under pressure, with zinc, while in the aromatic series, the chloro-, bromo-, or iodo-compound may be heated above its melting point, or in presence of a solvent such as nitrobenzene, with copper powder (Ullmann). The order of reactivity of the halogen is I $>$ Br $>$ Cl. Good yields are obtained when the halogen is activated by the presence of a nitro group in the *ortho*-position (A., 332, 38; 350, 83). Amino-halogen compounds cannot be condensed in this way. The same generalisations hold also in the naphthalene series. (J. C. S., 1931, 3176.)

$$RI + 2Cu + IR \longrightarrow R.R + Cu_2I_2.$$

The reaction is only applicable for the preparation of symmetrical compounds from mono-halogen derivatives.

PREPARATION 12.—**Diphenyl** (*Phenylbenzene*).

$$C_6H_5.C_6H_5. \qquad C_{12}H_{10}. \qquad 154.$$

20 gms. (2 mols.) of iodobenzene are heated with 20 gms. (excess) of copper powder for 3 hours in a sealed tube (see p. 41) to 230°. The contents of the tube are extracted with ether, and the filtered extract fractionated, the ether being removed on a water bath and the fraction 245°—255° retained and recrystallised from alcohol.

$$2C_6H_5I + 2Cu = C_6H_5.C_6H_5 + Cu_2I_2.$$

*Yield.*—80% theoretical (6 gms.). Colourless leaflets; soluble in hot alcohol; M.P. 70°—71°; B.P. 254°; D. $^{82}_{4}$ 0·9845. (B., 34, 2176.)

**Reaction VIII. Action of certain finely divided Metals on Diazonium Compounds in Alcohol or Acetic Anhydride Solution.**—This reaction is limited to the preparation of *s*-diaryl compounds. Copper, zinc, or iron powder may be used, but the former is, on the whole, the most satisfactory, especially when it has been freshly prepared according to Gattermann's

recipe. As with other "finely divided metal" reactions of this type there is a Sandmeyer analogue, but except in the case of nitro-compounds, the reaction then for the most part takes a different course (see Reaction CLXVI.).

The reaction proceeds smoothly in aqueous or absolute alcoholic, or in acetic anhydride solution. (B., 23, 1226; 28, 2049.) Its exact course has not been worked out, but it may be formulated as follows :—

$$RNH_2 \rightarrow RN_2SO_4H$$
$$2RN_2.SO_4H + Cu \rightarrow RR + 2N_2 + CuSO_4 + H_2SO_4.$$

PREPARATION 13.—**Diphenyl** (*Phenylbenzene*).

$C_6H_5.C_6H_5$. $C_{12}H_{10}$. 154.

31 gms. (2 mols.) of aniline dissolved in 150 c.cs. of water and 40 gms. (slight excess) of concentrated sulphuric acid are diazotised in the usual way (see p. 372) with 23 gms. (2 mols.) of sodium nitrite in 10% solution. The diazonium solution is treated with 100 gms. of 98% alcohol and 50 gms. (excess) of copper powder (p. 508) are added while the whole is well stirred (see p. 39). A vigorous evolution of nitrogen occurs, and by the end of the reaction the temperature has risen to 30° or 40°. The stirring is continued for an hour, and then the mixture is steam distilled. The distillate at first consists chiefly of alcohol with small amounts of an oil insoluble in water. Small portions of it are tested from time to time by dilution with water. When a solid precipitate is thus obtained, the distillate is separately collected until no more solid comes over. The distillate is then heated to 71° to melt the solid diphenyl; on cooling until solidification takes place, the still liquid portion is poured off. The product is almost pure, but may be recrystallised from alcohol.

100 gms. of zinc powder may be used instead of the copper. With it the best results are obtained by adding, first, 10 c.cs. of a cold saturated solution of copper sulphate, and then the zinc as above. Care must be taken in this case not to let the temperature rise above 30°—40°. Iron powder can also be employed.

*Yield.*—In each case 25% theoretical (6 gms.). Properties (see p. 65).

Diphenyl can also be obtained from diazobenzene sulphate by treating it with warm benzene (B., 26, 1997), but the method is not of much importance, except in so far as it illustrates the well-known reactivity of diazo-compounds. (B., 23, 1226; 28, 2049.)

**Reaction IX.** (*a*) **Action of Magnesium Alkyl or Aryl Halide on certain Alkyl or Aryl Halides in the presence of Absolute Ether** (Grignard). (C. 1906, II., 748.)—The Grignard reaction has perhaps a wider application than even the Friedel-Crafts or the diazo reaction. When an alkyl or aryl bromide or iodide is treated with magnesium powder, usually in presence of absolute ether, a magnesium alkyl or aryl halide is formed.

$$Mg + RI = RMgI.$$

The substance so formed can be treated with a large variety of reagents to give a correspondingly large number of compounds, provided there is no moisture present, the smallest trace of which completely inhibits

reaction. There are various theories to account for the action of the ether or the other solvents which can be used in its place. These will be found discussed in any large text-book on organic chemistry.

When alkyl halides act on an absolute ethereal solution of magnesium alkyl or aryl halide, hydrocarbons are formed.

$$RMgI + R_1I = RR_1 + MgI_2.$$

The same type of reaction occurs when magnesium acts on an excess of an alkyl or aryl halide in the presence of absolute ether. *n*-Hexyl bromide in this way yields *n*-dodecane.

$$C_6H_{13}.MgBr + C_6H_{13}Br = C_{12}H_{26} + MgBr_2.$$

For preparation of Grignard reagent without ether, see E.P., 398561.

Further applications of the Grignard reaction are given under Reactions XIV., XXII., XXXIV. (*b*), XLIII., LX. See also Ann. Rep., 1932, 99.

**Reaction IX.** (*b*) **Action of Heat on the Compound formed by treating Magnesium Alkyl or Aryl Halide with a Ketone in absolute Ethereal Solution** (Grignard). (B., 35, 2647.)—When the Grignard reagent is treated with a ketone, the following reaction occurs :—

$$RR_1CO + R_{11}MgI = RR_1R_{11}C.OMgI.$$

This latter compound when treated with water is hydrolysed to a tertiary alcohol $RR_1R_{11}COH$. If, however, the anhydrous reaction mixture be heated for a long time on the water bath, an olefine is formed with the splitting-off of magnesium hydroxyiodide.

$$CH_3I + Mg = CH_3.Mg.I.$$
$$CH_3.Mg.I. + C_6H_5.CO.CH_3 = (C_6H_5)(CH_3)_2C.O.Mg.I.$$
$$(C_6H_5)(CH_3)\overset{\overset{\textstyle CH_3}{|}}{C}.O.Mg.I = (C_6H_5)(CH_3).C : CH_2 + Mg(OH)I.$$

Acetophenone and magnesium methyl iodide yield 2-phenyl-l-propene. As can be seen from the equation, one at least of the radicals R, $R_1$, $R_{11}$, must have a non-tertiary carbon linked in the intermediate compound to the " hydroxy-magnesium-iodide " carbon.

PREPARATION 14.—αα-**Diphenylmethylethylene** (*αα-Diphenylpropene*).

$$(C_6H_5)_2C : CH.CH_3. \qquad C_{15}H_{14}. \qquad 194.$$

The Grignard reagent is prepared from 6 gms. (2 mols.) of dry magnesium, and 39 gms. (2 mols.) of ethyl iodide (redistilled), as described in Preparation 19, 120 c.cs. of anhydrous ether being used. 23 gms. (1 mol.) of dry, finely divided benzophenone are added, the flask being cooled if the reaction becomes too vigorous. The mixture is then heated 6 hours on a water bath, treated with dilute acid, extracted with ether, the ether removed on a water bath, and the residue fractionated under reduced pressure, the fraction 169°—170° at 18 mms. being separately collected and recrystallised from petroleum ether.

$$C_2H_5I + Mg \rightarrow C_2H_5.Mg.I.$$
$$C_2H_5.Mg.I + (C_6H_5)_2CO \rightarrow (C_6H_5)_2C(OMgI)CH_2CH_3.$$
$$(C_6H_5)_2C(OMgI)CH_2CH_3 \rightarrow (C_6H_5)_2C = CH.CH_3 + Mg(OH)I.$$

Colourless crystals ; M.P. 52° ; B.P. $^{18}$ 169°—170°. (B., 35, 2647.)

**Reaction IX.** (*c*) **Action of Dimethyl Sulphate on Magnesium Alkyl or Aryl Halide** (Grignard).—When a Grignard compound is treated with dimethyl sulphate, methylation of the alkyl or aryl group takes place, the metal-halogen residue being split off. (B., 36,2 116. See also O.S., XI., 66.)

$$R.Mg.Br + (CH_3)_2SO_4 = R.CH_3 + Br.Mg.(CH_3)SO_4.$$

Diethyl sulphate reacts similarly. (Am. Soc., 44, 2621.)

The yields are good, as is to be expected from the components of the reaction.

It will be noted that in the Grignard reactions so far described, only bromo- or iodo-compounds are mentioned. Chlorine compounds do not enter so readily into this reaction; to induce them to react it is usually necessary to add a crystal of iodine (B., 38, 2759), or mercuric chloride (C., 1907, I., 872), or a previously prepared magnesium solution (B., 38, 1746; C., 1907, I., 455), or a small amount of Gilman's catalyst (Rec., 1928, 47, 19), which is prepared by heating an alloy of Mg containing 12·75% of Cu with about 20% iodine *in vacuo.*

By the method above outlined, toluene has been prepared from bromobenzene, and *p*-xylene from *p*-bromotoluene.

PREPARATION 15.—*p*-**Xylene** (1 : 4-*Dimethylbenzene*).

$C_8H_{10}$. 106.

The Grignard reagent is prepared, as in Preparation 19, by heating 67 gms. (1 mol.) *p*-bromotoluene, 10 gms. (1 mol.) of dry magnesium and 200 c.cs. of anhydrous ether. When almost all the magnesium has disappeared a solution of 50 gms. (1 mol.) of dimethyl sulphate (caution !) in anhydrous ether is added. A vigorous reaction takes place, and after it subsides the reaction product is poured on to ice. The ether is removed by distillation, and the residue is steam distilled. The oil is separated from the distillate and fractionated, the fraction, 136°—140°, being collected.

$$CH_3C_6H_4Br \rightarrow CH_3C_6H_4MgBr \rightarrow CH_3.C_6H_4.CH_3.$$

*Yield.*—75% theoretical (30 gms.). Colourless oil: characteristic odour; B.P. 138°; D. $^{20}_{4}$ 0·869. (B., 36, 2116.)

Owing to the closeness of the boiling points of the three xylenes they cannot be readily separated one from the others; so that a method such as the above, by which one isomer can be obtained free from the others, in a good yield, is of importance. For some details on magnesium aryl halides, see B., 36, 2898, and O.S., X., 4.

*Note.*—Dialkyl sulphates are extremely poisonous; on no account must their vapour be inhaled. Work with them should be carried out in a good fume cupboard; they must be added to mixtures from a tap funnel, for if spilled on the hands they are absorbed through the skin. Should any fall on the clothes, these must be changed at once. See also p. 261.

**Reaction X.** (*a*) **Conversion of Simple Hydrocarbons, or Derivatives, into more Complex Hydrocarbons. Action of Zinc Alkyl on Alkyl Halides.**—The action of zinc alkyl on various types of compounds is much the same

as that of magnesium alkyl or aryl halide. Before the discovery of the latter, zinc alkyl was widely used as a general synthetic reagent, but its spontaneous inflammability led to its replacement by the more conveniently prepared Grignard reagent; it does not form aryl compounds; even in alkyl syntheses it is not nearly so widely applicable, its one advantage being that the reactions it does bring about go somewhat more smoothly than the corresponding magnesium reactions.

$$Zn(CH_3)_2 + 2CH_3I = ZnI_2 + 2C_2H_6.$$

**Reaction X.** (*b*) **Catalytic Conversion of Simple Hydrocarbons into more Complex Hydrocarbons.**—These reactions are usually accomplished at high temperatures in presence of catalysts. Acetylene, propylene and even methane can be converted into benzene. (E.P., 374,422; 369,351; 366,394.)

The reaction is of considerable industrial importance in dealing with gases evolved in processes of pyrolysis.

An interesting extension of the Friedel-Crafts' reaction, by which paraffins are converted into cyclo-paraffins, is described in B., 66, 1892. The reaction is summarised in A., 510, 269.

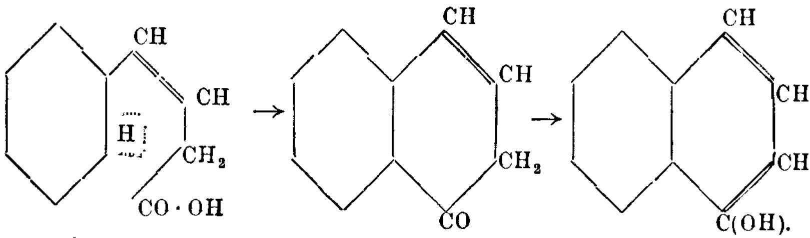
# CHAPTER IV

## CARBON TO CARBON

### Hydroxy Compounds

The condensations now to be considered include all those in which the reaction is such that there is of necessity a hydroxyl group in the final product.

**Reaction XI. Intramolecular Elimination of Water from certain Molecules.** (A., 227, 242.)—When phenyl isocrotonic acid is heated, water is eliminated and α-naphthol is formed. This synthesis, which is of theoretical interest, was discovered by Fittig. It is one of the proofs of the structure of naphthalene.



**Reaction XII. Reduction of Aldehydes and Ketones to Pinacones.** (B., 27, 456.)—When ketones are reduced to secondary alcohols, some intermolecular condensation usually also occurs, and a pinacone is formed.

$$2RR_1CO + 2H = RR_1C(OH).C(OH).RR_1.$$

This side reaction cannot be avoided when reducing aliphatic ketones, but in the aromatic series either product can be obtained by varying the conditions of the reduction. An alkaline reduction favours alcohol production; pinacones are formed when acid reducing agents are employed (see Preparation 16).

Pinacones can also be obtained by using suitable electrolytic reductions. Aldehydes, too, have been brought within the scope of the reaction. Thus hydrobenzoin [s-diphenyl-ethan-diol] has been prepared from benzaldehyde by an acid reduction.

$$2C_6H_5.CHO \rightarrow C_6H_5.CH(OH).CH(OH).C_6H_5.$$

Acetone, the simplest ketone, gives the simplest pinacone.

$$2(CH_3)_2CO \rightarrow (CH_3)_2C(OH)C(OH)(CH_3)_2.$$

The pinacones formed from acetophenone, benzophenone, and many

other ketones are exactly similar in structure (C., 1906, II., 148; B., 27, 454; C., 1900, II., 794; C., 1903, II., 23).

PREPARATION 16.—**Benzpinacone** (*αβ-Dihydroxy-tetraphenylethane*).

$$(C_6H_5)_2.C(OH).C(OH).(C_6H_5)_2. \quad C_{26}H_{22}O_2. \quad 366.$$

5 gms. (2 mols.) of benzophenone are boiled for ¼ hour with 50 gms. of 85% acetic acid and 10 gms. of zinc foil, the whole being well shaken throughout. The liquid is decanted from the zinc residues, cooled, and filtered; the filtrate is again boiled up with zinc, and this process repeated a third time, the same filter being used each time. The benzpinacone remaining on the filter is then washed with 85% acetic acid, and recrystallised from 13 parts of boiling glacial acetic acid.

*Yield.*—90% theoretical (4·5 gms.). Colourless crystals; M.P. (with decomposition) 168°. (C., 1881, 150; A., 133, 26; B., 10, 1473.)

For photochemical reduction of benzophenone to benzpinacone by means of isopropyl alcohol, see O.S., XIV., 8.

For the "pinacoline transformation" undergone by pinacones, see p. 79.

**Reaction XIII. Condensation of a Phenol with Formaldehyde** (Lederer-Manasse). (B., 27, 2411.)—This reaction can take three different courses according to conditions.

(i.) With the more powerful condensing agents, *e.g.*, caustic alkalis or hydrochloric acid, a diphenylmethane compound is usually formed.

$$2C_6H_5OH + H.CHO = HO.C_6H_4.CH_2.C_6H_4OH + H_2O.$$

(ii.) The less powerful condensing agents, *e.g.*, alkali carbonates, alkaline earth oxides, lead oxide, or dilute acids or alkalis, give a benzyl alcohol or sometimes a di-(hydroxy-methyl) compound.

$$C_6H_5OH + H.CHO = OH.C_6H_4.CH_2OH$$
$$C_6H_4(CH_3)(OH)[1:4] + 2H.CHO = C_6H_2(CH_3)(OH)(CH_2OH)_2[1:4:3:5].$$

(iii.) Hydrochloric acid sometimes gives a benzyl chloride derivative, the benzyl alcohol first formed being chlorinated by the acid. Such chlorides are easily hydrolysed to the alcohol (see Preparation 126).

$$OHC_6H_4.Cl[1:2] + H.CHO \longrightarrow C_6H_3(OH)(Cl)(CH_2OH)[1:2:4]$$
$$\longrightarrow C_6H_3(OH)(Cl)(CH_2Cl)[1:2:4].$$

In all three cases the *para*-position to the hydroxyl group is preferred; if it is occupied, condensation takes place, but less readily, in the *ortho*-. The above rules as to which condensation a given reagent will bring about are only general, in no particular case can it be foretold with certainty how far the reaction will go.

The reaction is of importance, especially when as in (ii.) it is used for the production of phenolic methanols. Formaldehyde, when condensed with phenols in presence of acid or basic catalysts, yields resinous substances, which, when dehydrated under pressure, yield hard resinoids (Bakelite, Novolak). (See J. S. C. I. (C. & I.), 1937, 103).

For other formaldehyde condensations, see Reactions XIX. (*b*), XXXIII. (*a*).

PREPARATION 17.—*o*- and *p*-**Hydroxybenzyl Alcohols** (1 : 2- and 1 : 4-*Methylolhydroxybenzenes*).

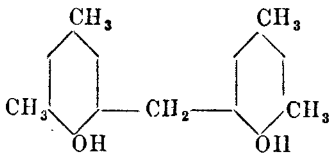
$C_6H_4.(OH)(CH_2OH)$. $C_7H_8O_2$. 124.

30 gms. (1 mol.) of phenol are dissolved in 150 c.c. (a slight excess) of 10% caustic soda; 35 gms. (excess) of 40% formaldehyde solution are added, and the whole allowed to remain at room temperature for 6 days. It is neutralised with hydrochloric acid, extracted repeatedly with ether, and the latter removed on a water bath. If necessary the residue is steam distilled to remove unchanged phenol, and the benzyl alcohols which are left are then shaken for some time with cold benzene until nothing further dissolves. The *ortho*-compound, which is much the more soluble, is thus separated from the *para*-.

$$C_6H_5(OH) + H.CHO = OH.C_6H_4.CH_2OH.$$

*Yield.*—Including both compounds, 80% theoretical (32 gms.). *o*-Hydroxybenzyl alcohol (saligenin) forms colourless crystals; M.P. 82°; the *para*-compound melts at 112°. (B., 27, 2411.)

PREPARATION 18.—3 : 5 : 3′ : 5′-**Tetramethyl**-2 : 2′-**Dihydroxydiphenylmethane.**




$C_{17}H_{20}O_2$. 256.

10 gms. (2 mols.) of xylenol (1 : 3-dimethyl-4-hydroxybenzene) are dissolved in 300 c.cs. (excess) of 1·5% caustic soda solution; 5 gms. (excess) of 40% formaldehyde solution are added, and the mixture allowed to stand for 4 days. It is then acidified with acetic acid and extracted with ether, the solvent removed on a water bath, and the residual oil left in a vacuum over sulphuric acid until at length it becomes almost a solid. The latter is recrystallised several times from ligroin.

$$2C_6H_3(CH_3)_2(OH)[1:3:4] + CH_2O = [3:5:6]C_6H_2(CH_3)_2(OH).CH_2.C_6H_2—(CH_3)_2(OH)[3':5':6'] + H_2O.$$

Long colourless needles; easily soluble in alcohol, ether, chloroform, acetic acid, benzene; sparingly soluble in cold ligroin; M.P. 145°—146°; when boiled for 1 hour with acetic anhydride a diacetate is obtained which when recrystallised from dilute alcohol forms fine needles, M.P. 86°. (B., 40, 2526.)

**Reaction XIV.** (*a*) **Action of Magnesium Alkyl or Aryl Halide on Aldehydes and Ketones** (Grignard). (B., 31, 1003.)—This phase of the Grignard reaction can be utilised for the preparation of all types of alcohols (C., 1901, I., 725; II., 622; 1902, I., 414).

(i.) Primary alcohols can be obtained from formaldehyde, or rather from its polymer trioxymethylene, which has to be used in place of the usual aqueous solution. Magnesium phenyl iodide and trioxymethylene

yield benzyl alcohol for example, the usual Grignard intermediate compound being formed.

$$C_6H_5MgI + CH_2O \rightarrow H_2C(C_6H_5)OMgI \rightarrow C_6H_5CH_2OH.$$

(ii.) Other aldehydes yield in the same way secondary alcohols.
Acetaldehyde and methyl iodide give isopropyl alcohol.

$$CH_3CHO + MgCH_3I \rightarrow (CH_3)C(CH_3)OMgI \rightarrow (CH_3)_2CHOH.$$

Benzaldehyde and magnesium phenyl bromide or iodide give diphenyl carbinol.

$$C_6H_5CHO + MgC_6H_5I \rightarrow (C_6H_5)_2CHOMgI \rightarrow (C_6H_5)_2CHOH.$$

(C.r., 130, 1322 ; B., 31, 1003.)

(iii.) Tertiary alcohols are formed from ketones.

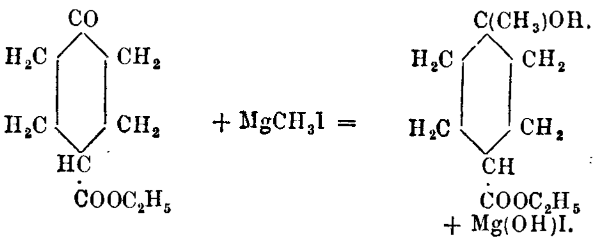
The simplest tertiary alcohol is prepared from acetone and magnesium methyl iodide.

$$Mg(CH_3)I + (CH_3)_2CO \rightarrow (CH_3)_2C(CH_3)OMgI \rightarrow (CH_3)_3C(OH).$$

Methyl ethyl ketone and methyl iodide give tertiary amyl alcohol.

$$CH_3COC_2H_5 + CH_3MgI = (CH_3)_2.C(OH).C_2H_5 + Mg(OH)I.$$

In the aromatic series, acetophenone and methyl iodide, for example, yield phenyldimethylcarbinol. An important step in the synthesis of *i*-terpineol is the preparation of ethyl-δ-hydroxy-hexahydro-*p*-toluate from ethyl-δ-ketohexahydrobenzoate and magnesium methyl iodide.




The usual precautions must be taken in all these reactions, to guard against the possibility of moisture being present. The technique of the method will be apparent from the following.

Preparation 19.—**Phenylmethylcarbinol** (1-*Phenyl*-1-*ethanol*).

$$HC(CH_3)(C_6H_5)OH. \qquad C_8H_{10}O. \quad 122.$$

All reagents used must be thoroughly dry.

(1.) 36 gms. (1 mol.) of methyl iodide which have been allowed to stand for 12 hours over calcium chloride and then redistilled, are mixed with 50 c.cs. of ether purified and dried as described on p. 216. 20 c.cs. of this mixture are run into a flask fitted with a dropping funnel and long reflux condenser. The flask contains 6 gms. (1 mol.) of magnesium ribbon, which has been cleaned with emery paper, washed with ether, and dried

in an air oven at 110°. If necessary, the reaction is started by adding a crystal of iodine. When the first reaction has subsided, 70 c.cs. of dry ether are added, and the remainder of the mixture of alkyl iodide and ether run in drop by drop from the tap funnel. The contents of the flask are then boiled on the water bath until all (or nearly all) of the magnesium has dissolved. E.P., 398561 describes preparation without ether.

(2.) The flask is now disconnected, and under cooling by ice-water, 26 gms. (1 mol.) of freshly distilled benzaldehyde mixed with an equal volume of dry ether are dropped in from a tap funnel with constant shaking, and the whole allowed to stand for 12 hours.

(3.) Just sufficient hydrochloric acid to dissolve the precipitate is added with constant shaking and cooling. The aqueous layer is separated, and the ether washed first with sodium bicarbonate solution, then with sodium bisulphite (to remove free iodine) and again with sodium bicarbonate. The extract is dried over potassium carbonate and the ether removed on a water bath. The carbinol which remains is fractionated under reduced pressure.

(1) $CH_3I + Mg = CH_3MgI$.
(2) $C_6H_5CHO + CH_3MgI = C_6H_5(CH_3)CH(OMgI)$.
(3) $(C_6H_5)(CH_3)CH(OMgI) + H_2O = (C_6H_5)(CH_3)CHOH + (OH)MgI$.

*Yield.*—56% theoretical (20 gms.). Colourless liquid; insoluble in water; B.P. $^{15}$ 100°; B.P. $^{28}$ 110°—111°; B.P. $^{40}$ 118°; B.P. $^{760}$ 203°; D.$^{15}_{4}$ 1·013. (C. r., 130, 1322; B., 31, 1003.)

The same method may be used for phenylethyl carbinol taking 39 gms. (1 mol.) of ethyl iodide. The compound is obtained as a colourless liquid; B.P. $^{760}$ 221°; D. $^{15}_{4}$ 0·9900.

PREPARATION 20.—*tert.*-**Butyl Alcohol** (*Trimethylcarbinol*).

$(CH_3)_3C(OH)$. $C_4H_{10}O$. 74.

The Grignard compound is prepared as described in Preparation 19 from 36 gms. (1 mol.) of dry methyl iodide, 120 c.c. of sodium-dried ether, and 6 gms. (1 mol.) of dry magnesium ribbon or powder. 14 gms. (1 mol.) of *dry* acetone dissolved in 30 c.c. of *dry* ether are slowly added from a tap funnel with constant shaking and under cooling by ice-water. A white bulky precipitate of the magnesium compound separates. After standing overnight, just sufficient dilute sulphuric acid to dissolve the precipitate is added with constant shaking and cooling. The ether solution of the alcohol separates and is withdrawn and distilled.

$$(CH_3)_2CO + Mg.CH_3.I = (CH_3)_2C(CH_3).OMgI.$$
$$(CH_3)_3C(OMgI) + H_2O + (CH_3)_3C(OH) + Mg(OH)I.$$

Colourless crystals; soluble in water; M.P. 25°; B.P. 83°; D. $^{30}_{4}$ 0·7788.

In an exactly similar manner dimethylethylcarbinol may be prepared from ethyl iodide. It is obtained as a colourless liquid, soluble in water; B.P. $^{762}$ 102°; D. $^{15}_{4}$ 0·8144.

The following shows the method of preparing and using magnesium aryl halides in this synthesis.

PREPARATION 21.—**Triphenylcarbinol** (*Triphenylmethanol*).

$(C_6H_5)_3C(OH)$. $C_{19}H_{16}O$. 260.

1·2 gms. (1 mol.) of bright magnesium ribbon is dried in the air oven at 110°, cut into 1 cm. pieces, and treated in a well-dried round-bottomed 300-c.c. flask with a solution of 8 gms. (1 mol.) of bromobenzene in 40 gms. of sodium-dried ether to which a crystal of iodine has been added. The flask is now warmed on a water bath, under a reflux condenser in a current of dry hydrogen (caution! no flame must approach the end of the condenser). Light flocculæ appear in the liquid; they are due to unavoidable moisture, but they soon disappear, and then the magnesium begins to dissolve. When the magnesium has completely dissolved, except for traces of impurities—this should not take more than 2 hours—the heating is stopped, and the liquid is treated at ordinary temperatures with 9·1 gms. (1 mol.) of benzophenone dissolved in 25 gms. of sodium-dried ether. The liquid becomes red, then a thick tough precipitate separates, which, when the heating is renewed, reacts vigorously, and solidifies in the course of half an hour. The reaction mixture is then allowed to cool, and treated with pieces of ice and sulphuric acid. When decomposition is complete, steam is passed through until the distillate is clear. This removes ether and all by-products (benzene, diphenyl); almost pure triphenylcarbinol remains, and is recrystallised from benzene.

$$C_6H_5.Br + Mg = C_6H_5.Mg.Br.$$
$$C_6H_5.MgBr + C_6H_5.CO.C_6H_5 = (C_6H_5)_2C(C_6H_5)OMgBr.$$
$$(C_6H_5)_2C(C_6H_5)(OMgBr) + H_2O = (C_6H_5)_3C.OH + OH.Mg.Br.$$

*Yield.*—75% theoretical (10 gms.). Colourless crystals; soluble in ether and hot benzene; gives a deep red solution in strong sulphuric acid; in glacial acetic acid it is colourless, but addition of a drop of concentrated hydrochloric acid gives a deep yellow coloration; M.P. 159°.

Diphenylmethylcarbinol is prepared in the same way from acetophenone.

**Reaction XIV.** (*b*) **Action of Magnesium Alkyl or Aryl Halide on Esters, Acyl Chlorides, and Acid Anhydrides.** (C., 1901, I., 725; II., 622; 1902, I., 1414.)—In all the above cases tertiary alcohols are obtained, except, of course, in the case of formic esters when secondary alcohols are formed. Using esters, the reaction has a wide application, as the examples given below show; the use of the acyl chlorides and anhydrides is only of theoretical interest. The reactions in all cases take the usual "Grignard" course.

$$RCOOC_2H_5 + 2MgR_1Br \rightarrow R(R_1)_2COMgBr + Mg(OC_2H_5)Br.$$

$$RC(R_1)_2OMgBr + H_2O \rightarrow R(R_1)_2C(OH) + Mg(OH)Br.$$

$$RCOCl + 2MgR_1Br \rightarrow RC(R_1)_2OMgBr + MgBrCl.$$

$$(RCO)_2O + 4MgR_1Br \rightarrow 2R(R_1)_2COMgBr + (MgBr)_2O.$$

$$2R(R_1)_2COMgBr + H_2O \rightarrow 2R(R_1)_2C(OH) + (MgBr)_2O.$$

The yields are in most cases good, and the reactions smooth. A great advantage of the Grignard reaction is that it can be applied to complicated derivatives of the reacting substances. This renders it valuable in the synthesis of substances such as, *e.g.*, terpenes. The following list should give some idea of the scope of the reaction :—

(i.) Ethyl formate and magnesium ethyl iodide give diethyl carbinol.

(ii.) Methyl acetate and magnesium methyl iodide give tertiary butyl alcohol (*cf.* Reaction XIV. (*a*) (iii.) ).

(iii.) Ethyl $\Delta'$-tetrahydro-*p*-toluate, see p. 73, and magnesium methyl iodide give *i*-terpineol.

(iv.) Ethyl chloracetate and magnesium phenyl bromide give diphenylchlorohydrin.

(v.) Methyl benzoate and magnesium phenyl bromide give triphenyl carbinol.

(vi.) Acetyl chloride and magnesium methyl iodide give trimethyl carbinol.

(vii.) Acetic anhydride and magnesium ethyl iodide give diethylmethyl carbinol.

The equations of the above reactions should be written out. An interesting application of the method such as contained in (iii.) should be looked up in the original literature.

It may be mentioned that the " Grignard " reaction can also be applied to the production of primary alcohols by the interaction of ethylene oxide and magnesium alkyl halide.

$$\left.\begin{array}{l} CH_2 \\ | \\ CH_2 \end{array}\right\rangle O + MgBrC_2H_5 \rightarrow \begin{array}{l} CH_2—OMgBr \\ | \\ CH_2—CH_2—CH_3 \end{array} \rightarrow \begin{array}{l} CH_2—OH \\ | \\ CH_2—CH_2—CH_3. \end{array}$$

PREPARATION 22.—**Triphenylcarbinol** (*Triphenylmethanol*).

$(C_6H_5)_3C(OH)$. $C_{19}H_{16}O$. 260.

The Grignard reagent—magnesium phenyl bromide—is prepared as described in Preparation 21 from 1·2 gms. (1 mol.) of dry magnesium and 8 gms. (1 mol.) of dry bromobenzene. 6·8 gms. (1 mol.) of dry methyl benzoate dissolved in 25 gms. of sodium-dried ether are added to the cold solution, slowly; and with constant shaking. The liquid is then heated on a water bath until no further change takes place. Ice and dilute sulphuric acid are added to the cold reaction mixture, which, when the precipitate has dissolved, is steam distilled. The triphenyl carbinol which remains is recrystallised from benzene.

$$C_6H_5COOCH_3 + 2C_6H_5MgBr \rightarrow (C_6H_5)_3C.O.MgBr \rightarrow (C_6H_5)_3C(OH).$$

See p. 75.

**Reaction XV. Action of Zinc Alkyl on Aldehydes, on certain Ketones, and on Acyl Chlorides.** (A., 223, 162.)—As with other " zinc alkyl " reactions the corresponding Grignard reaction described in Reaction XIV. has replaced it almost completely, so that the following is only of more or less historical and theoretical interest :

(*a*) With *all* aldehydes, except formaldehyde, secondary alcohols are formed (A., 213, 369 ; B., 14, 2557).

$$CH_2CHO \rightarrow (CH_3)_2CHOZnCH_3 \xrightarrow{H_2O} (CH_3)_2CHOH.$$

This reaction only occurs with zinc methyl and zinc ethyl ; with the higher zinc alkyls the aldehydes are reduced to the corresponding alcohols (B.. 17, R., 318 ; A., 223, 162).

(*b*) In general ketones do not react with zinc alkyl. Exceptions are certain ketones which do not contain a methyl group attached to the carbonyl group, *e.g.*, diethyl ketone, ethylpropyl ketone. These with zinc methyl or ethyl yield the usual zinc-oxy-alkyl compounds which, when treated with water, give tertiary alcohols (B., 19, 60 ; 21, R., 55).

$$(C_2H_5)_2CO \rightarrow (C_2H_5)_3COZnC_2H_5 \xrightarrow{H_2O} (C_2H_5)_3C(OH).$$

(*c*) With acid chlorides the reaction takes place in two stages.

(i) One molecule of the zinc alkyl reacts and the usual type of addition compound is formed.

$$CH_3COCl + Zn(CH_2)_2 \rightarrow (CH_2)_2\overset{Cl}{\overset{/}{C}}OZnCH_2.$$

If water be now added, a ketone is obtained.

(ii.) If a second molecule of the zinc alkyl acts upon the new compound, another reaction takes place.

$$(CH_2)_2C(Cl)(OZnCH_3) + Zn(CH_2)_2 \rightarrow (CH_3)_2COZnCH_3 + Zn(CH_3)(Cl).$$

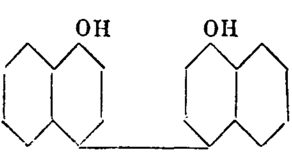
Addition of water yields now a tertiary alcohol.

$$(CH_3)_3C(O.Zn.CH_3) \xrightarrow{H_2O} (CH_3)_2C(OH).$$

If in the second stage another zinc alkyl be used, tertiary alcohols containing two or three different alkyl groups can be prepared (A., 175, 374 ; 188, 110, 122 ; C., 1910, II., 1201). Only zinc methyl and zinc ethyl thus furnish tertiary alcohols ; zinc propyl produces only those of the secondary type (B., 16, 2284 ; 24, R., 667). The historical importance of the acid chloride method lies in the fact that in 1864 it led to the discovery of tertiary alcohols.

**Reaction XVI. Action of certain Oxidising Agents on α- and β-Naphthols.** (J. R. C. S., 6, 183.)—If to an aqueous solution of a naphthol a few drops of a neutral aqueous solution of ferric chloride be added, a green coloration is produced, and, after a time, a flocculent precipitate of dinaphthol. Performed in this way on the " test tube " scale, the reaction is very useful for identification purposes.

PREPARATION 23.—αα-**Dinaphthol** (4 : 4′-*Dihydroxy*-1 : 1′-*dinaphthyl*).




$C_{20}H_{14}O_2$. 286.

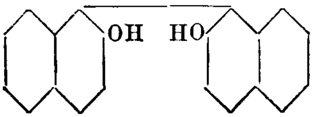
10 gms. (2 mols.) of α-naphthol are dissolved in the minimum quantity of boiling water, and ferric chloride solution is gradually added on cooling, until the precipitate formed is a bright reddish-violet. The latter is filtered off, and is boiled once with water, and twice with benzene. The residue is recrystallised from alcohol.

$$2C_{10}H_7OH + O = OH.C_{10}H_6.C_{10}H_6.OH + H_2O.$$

*Yield.*—35—40% theoretical (7—8 gms.). Shining rhombic crystals; insoluble in water; soluble in alcohol and ether; slightly soluble in chloroform and benzene; M.P. 300°. (J. R. C. S., 6, 183.)

A solution of α-naphthol in very dilute alcohol can also be used in the above preparation.

PREPARATION 24.—**ββ-Dinaphthol** (2 : 2′-*Dihydroxy*-1 : 1′-*dinaphthyl*).




$C_{20}H_{14}O_2$. 286.

10 gms. (2 mols.) of β-naphthol are dissolved in an excess of ether, and 16 gms. (excess) of anhydrous ferric chloride are gradually added to the solution in a flask fitted with a reflux condenser. Much heat is evolved during this operation. The mixture is then refluxed on a water bath until most of the naphthol is oxidised. (To test this a small portion of the ethereal solution is treated with an excess of dilute hydrochloric acid, and the ether evaporated. The dinaphthol separates out even in the warm as an oil while β-naphthol crystallises out on cooling.) When this is the case, the ether is removed on a water bath, water and powdered calcium carbonate are added to the residue, and the whole well shaken. Excess caustic soda is then added, the solution is filtered and precipitated with dilute sulphuric acid. The precipitate is washed with boiling water or boiling ligroin, and recrystallised from benzene.

$$2C_{10}H_7OH + 2FeCl_3 = OH.C_{10}H_6.C_{10}H_6.OH + 2FeCl_2 + 2HCl.$$

*Yield.*—40% theoretical (8 gms.). Colourless needles from alcohol, prisms from a mixture of carbon disulphide and alcohol; insoluble in water; slightly soluble in chloroform; soluble in alcohol and ether; M.P. 216°; M.P. (corr.) 218°; Forms a picrate. (J. R. C. S., 6, 187; B., 15, 2166.)

# CHAPTER V

## CARBON TO CARBON

### Oxy Compounds

In the following section are discussed the more important of those condensations which give rise to oxy compounds—aldehydes, ketones, and quinones. The reactions in this section may be divided into two classes—those in which the product is an oxy compound, because oxy compounds only undergo the reaction—the oxy group playing, so to speak, a catalytic part, *e.g.*, Reaction XX. (*b*); and those in which an oxy compound is actually formed during the action from non-oxy starting substances, *e.g.*, Reaction XVII.

Owing to the peculiar activating properties of the oxy group, the former reaction is more important than those discussed in the previous section.

**Reaction XVII. Intramolecular Rearrangement of the Glycols (Pinacoline Transformation).** (B., 36 2016.)—Di-primary, primary-secondary, primary-tertiary, and di-secondary glycols yield aldehydes by withdrawal of water and rearrangement, when heated with hydrochloric or sulphuric acids, or with certain dehydrating agents. Ethylene oxide derivatives may be considered to be intermediate compounds, for the ethylene oxide compounds themselves undergo the same change.

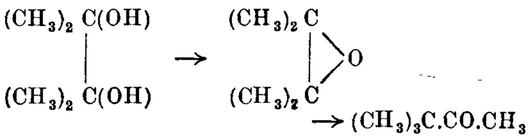
Hydrobenzoin yields diphenylacetaldehyde.

$$C_6H_5.CH(OH).CH(OH).C_6H_5 \rightarrow C_6H_5.\underset{\diagdown\,O\,\diagup}{CH.CH}.C_6H_5 \rightarrow (C_6H_5)_2.CH.CHO.$$

(C., 1907, I., 15; B., 36, 2016.)

Secondary-tertiary and di-tertiary glycols change into ketones in the same way, similar elimination of water and migration of an alkyl group occurring.

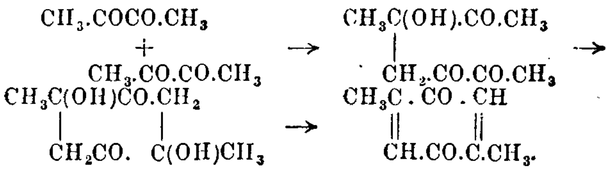
The di-tertiary glycols—known as "pinacones"—undergo this reaction with great readiness, yielding ketones—"pinacolines." The simplest of the di-tertiary glycols is tetramethyl glycol or pinacone, and this, by the transformation, gives pinacoline. (C., 1906, II., 670.)



The reaction itself is called the "pinacoline transformation." Ethers of the glycols also behave similarly, in some cases with particular ease (B., 39, 2288; A., Ch. (8), 9, 484). For a corresponding reaction among ketones, see p. 111. See also Ann. Rep., 1930, 114.

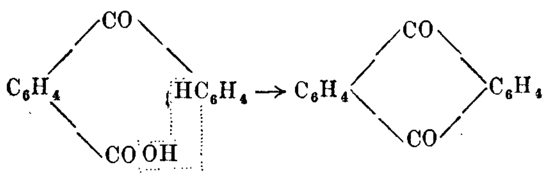
**Reaction XVIII. Ring Formation by Elimination of Water from certain Molecules.** (B., 41, 3632, ; A., 311, 178.)—Many important syntheses of ring compounds come under this heading. Only a few can be mentioned.

(i.) 1 : 2-Diketones containing a $CH_2$ group together with the CO group can be condensed to quinone derivatives—diacetyl, for example, readily yields dimethyl quinone—under the action of alkalis; ketols are intermediately formed.



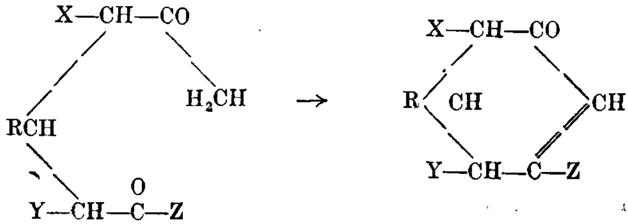
(B., 22, 2215 ; 28, 1845.)

(ii.) The *o*-benzoylbenzoic acids give anthraquinone derivatives on heating with dehydrating agents. This synthesis is very similar to that of *a*-naphthol from phenyl-*iso*-crotonic acid (Reaction XI.), but there is no rearrangement of the primary product. (Z. a., 19, 669.)

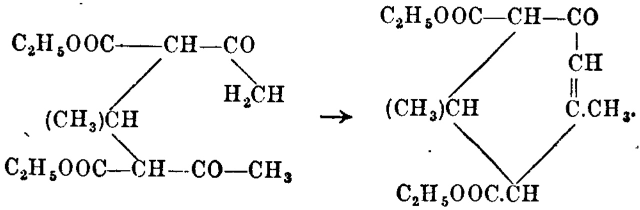


*o*-Benzoylbenzoic acid (Reaction XXXV. (*a*) ) itself yields anthraquinone, and 2-*p*-toluoylbenzoic acid gives 2-methyl-anthraquinone. These syntheses are of theoretical interest in throwing light on the structure of anthraquinone and hence of anthracene, and many of them are of considerable industrial importance (see Reaction XX. (*a*), also Preparation 25).

(iii.) When ethylidene bisacetoacetic ester is refluxed with conc. sulphuric acid, simultaneous condensation to a ring compound, hydrolysis, and elimination of carbon dioxide take place, and a cyclic ketone is obtained. All compounds which, like ethylidene bisacetoacetic ester, contain 1 : 5-carbonyl groups, and in addition a methyl group attached to one of them, undergo the same condensation with acids or alkalis, so that there exists here a very general method of passing from open-chain to ring compounds. To take the most general case—



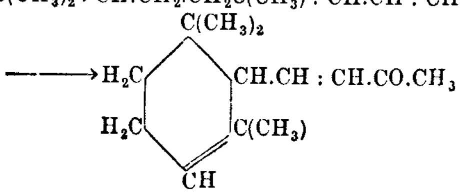
In the example given above—



A further reaction then takes place in this particular instance (see Preparation 26), but in the general case the reaction goes no further. The compounds so obtained are all derivatives of cyclohexenone. These latter compounds may be transformed by various reactions into cycloparaffins on the one hand, and aromatic compounds on the other. This affords a method of passing from simple aliphatic to aromatic compounds (see Preparation 446). (A., 281, 25.)

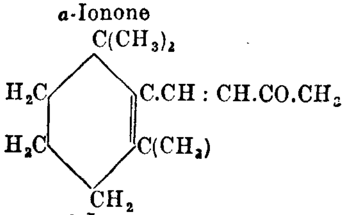
(iv.) The last example is the final step in the all but successful attempt of Tiemann and Krüger to synthesise the natural perfume "irone"—the odoriferous principle of the iris root and also, probably, of the violet. Having obtained a pseudo-ionone (Reaction XXIV. (ii.)), these two chemists treated it with sulphuric acid and obtained two ring compounds, $\alpha$- and $\beta$-ionone—each an isomeride of irone (B., 26, 2675).

$C(CH_3)_2 : CH.CH_2.CH_2C(CH_3) : CH.CH : CHCOCH_3$



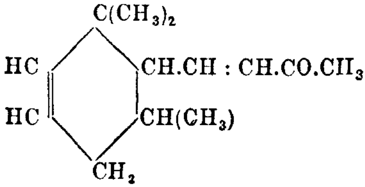
$\alpha$-Ionone

and

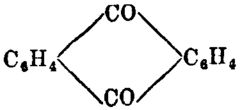


$\beta$-Ionone.

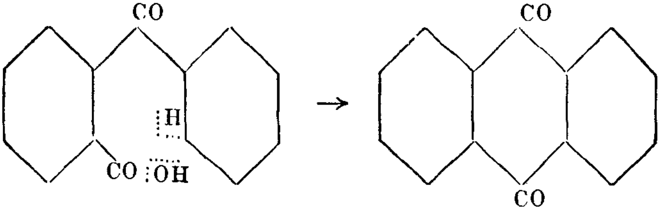
These compounds have an odour of violets, and are used in the manufacture of violet essence. Irone itself has the formula—



PREPARATION 25.—**Anthraquinone.**

 $C_{14}H_8O_2$. 208.

10 gms. (1 mol.) of *o*-benzoylbenzoic acid are mixed with 60 gms. of conc. sulphuric acid, heated to 150° for 1 hour, cooled and poured on to ice. The precipitated anthraquinone is collected and thoroughly washed, first with hot water, then with warm dilute (5 N) caustic soda and finally with warm water. It is dried in a steam oven, and completely purified by sublimation, at 250° (see p. 31).

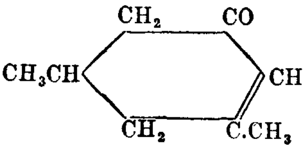


*Yield.*—Theoretical (9 gms.). Yellow needles; insoluble in water; somewhat soluble in benzene and the usual organic solvents; soluble in glacial acetic acid; M.P. 277°; sublimes at 250°; B.P. 382°. (Z. a., 19, 669.)

In the above preparation phosphorous pentoxide can equally well be used instead of sulphuric acid.

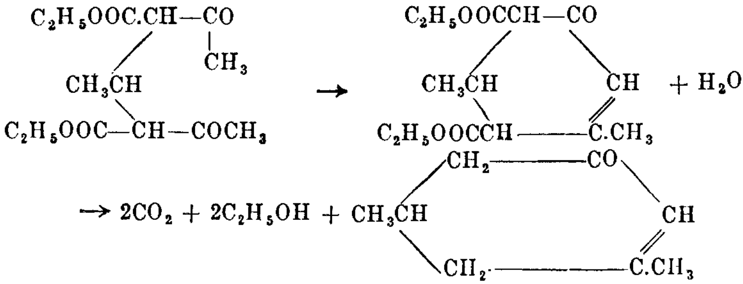
2-Methylanthraquinone can be prepared by heating 2-*p*-toluoylbenzoic acid with about 9 times its weight of oleum containing 20% $SO_3$. On dilution with water, and recrystallising from dilute acetic acid, pale yellow needles are obtained, M.P. 177°. (B., 41, 3632; J. pr. [ii], 33, 318; A., 311, 178).

PREPARATION 26.—1 : 3-**Dimethyl-$\Delta^6$-cyclohexen-5-one.**

 $C_8H_{12}O$. 124.

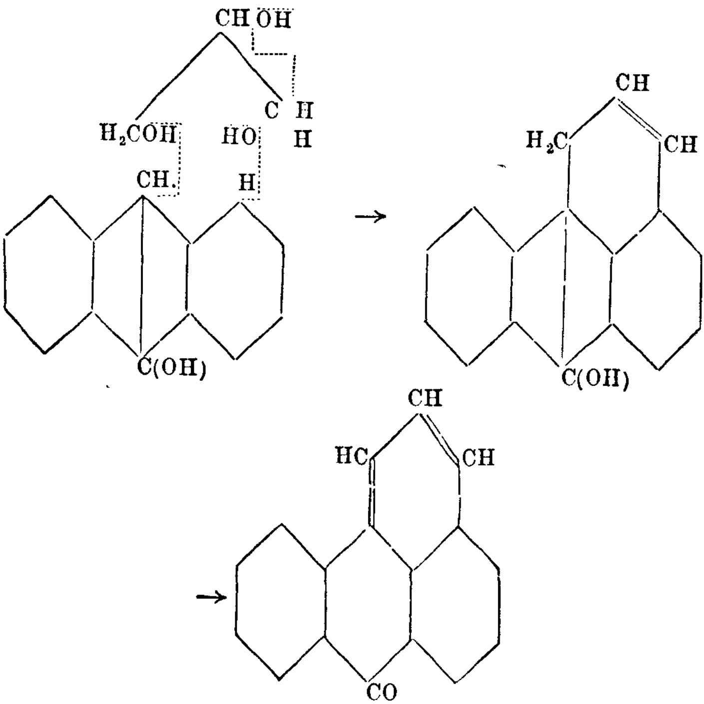
Crude ethylidinebisacetoacetic ester as prepared in Preparation 74 is melted on the water bath and poured into 500 c.cs. 20% sulphuric acid in a round-bottomed flask attached to a reflux condenser. A few pieces of porcelain chips are added, and the whole vigorously boiled for 7 hours. It is then steam distilled until the distillate measures about 100 c.cs. The distillate is then set aside in a well-stoppered bottle. The residue is again refluxed for 7 hours and again steam distilled, 100 c.cs. of distillate being again collected. The process is repeated a third time, and then steam is blown into the mixture until no oil, or only a trace, separates from a test portion when treated with solid caustic potash. To the three united

distillates solid caustic potash is carefully added until the solution is saturated. A reddish-brown oil separates, and is removed by means of a separating funnel. The alcohol is distilled off, using a column, and the residue dried over anhydrous sodium sulphate. The dimethylcyclohexenone is then recovered from the residue by fractional distillation, the fraction 200°—215° being retained.




*Yield.*—75—90% theoretical (15—18 gms.). Colourless liquid, B.P. 211°. (A., 281, 111.)

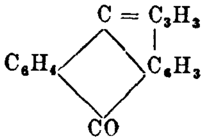
**Reaction XIX.** (*a*) **Condensation of Anthranol Derivatives with Glycerol.** (B., 44, 1666.)—This condensation gives rise to the benzanthrones which are used as intermediates in the dye industry. The reaction may be assumed to go as follows :—




Benzanthrone.

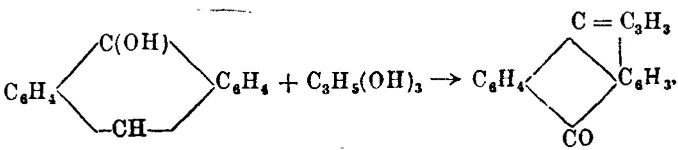
Sulphuric acid is the condensing agent used. The reaction might be compared with the preceding reaction and with Skraup's quinoline synthesis (see p. 165).

PREPARATION 27.—**Benzanthrone.**



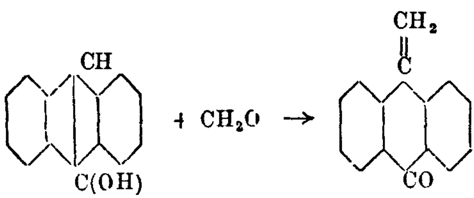
$C_{17}H_{10}O$. 230.

10 gms. (1 mol.) of anthranol are dissolved or suspended in 150 gms. of sulphuric acid (80%), and 10 gms. (excess) of glycerol are added. The mixture is carefully heated to 120°, when $SO_2$ is evolved, and kept there till the reaction is complete (4 hours). The cooled mass is poured into water, and the product which separates is collected, washed, boiled for 30 minutes with 13 times the quantity of 1% sodium hydroxide solution, pressed and dried. It is recrystallised from alcohol.



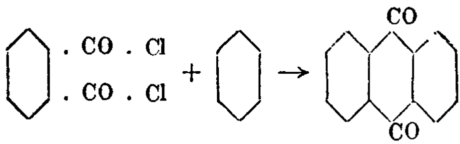
Pale yellow needles; insoluble in cold alcohol and in dilute acids and alkalis; soluble in conc. sulphuric acid with a reddish-brown colour, and deep orange fluorescence; M.P. 170°. (D.R.P. 176018; see also B., 44, 1666; O.S., XIV., 4; U.S.P., 1791309.)

**Reaction XIX.** (*b*) **Condensation of Anthranol Derivatives with Formaldehyde.** (A., 420, 134.)—The anthranols can also give rise to other intermediates by condensation with formaldehyde. Methylene anthraquinone is thus obtained from anthranol.



**Reaction XX.** (*a*) **Action of Metallic Zinc on a Mixture of an Aromatic Hydrocarbon and a Derivative of Phthalyl Chloride.**—This is a method of synthesising anthraquinone and its derivatives, and hence a method of elucidating their structure, and also the structure of anthracene. Otherwise the method is not of importance, but it may be in the future, since anthraquinone is in great and increasing demand for the production of vat-dyestuffs, such as indanthrene; phthalyl chloride can

be obtained cheaply from naphthalenes. (See also Reaction XX. (*b*) (vi).)



The action of zinc in this case resembles that of anhydrous aluminium chloride in the Friedel-Crafts reaction. Phthalyl chloride here reacts in the *s*- form (*cf.* Reaction XX. (*b*) (vi. ) ). Both forms have been prepared (A., 392, 245; M., 40, 81). The *s*- form melts at 15°—16°, the *as*- at 88°—89°, while both boil at 275° at 720 mms. The *s*- form is converted into the *as*- by the action of aluminium chloride, while the reverse change is effected by the action of heat or of hydrogen chloride. (B., 55, 1305.)

**Reaction XX.** (*b*) **Action of certain Anhydrous Metallic Halides (Aluminium Chloride, Aluminium Bromide, Aluminium and Hydrogen Chloride, Ferric Chloride) on a mixture of an Aromatic Hydrocarbon or certain Derivatives, and an Acyl Halide.** (Friedel-Crafts.) (A. Ch., [6], 1, 518.)—This is an even more important application of the Friedel-Crafts synthesis than the methods of synthesising hydrocarbons (pp. 58, 60). The reactions involved are more readily controlled since the products, in presence of aluminium chloride, do not undergo further condensations. Usually these products have also the advantage of being more easily separated, for, as shown below in (iii.), the formation of isomers can be avoided.

What has been said under Reaction VI. covers the general experimental methods of the synthesis, the same solvents and considerations applying in all cases. The following will give some idea of the scope of the reaction.

(i.) Both aliphatic and aromatic acyl chlorides can be used (A. Ch., [6], 1, 503 ; 14, 455).

$$C_6H_6 + CH_3COCl = C_6H_5.CO.CH_3 + HCl.$$
$$C_6H_6 + C_6H_5COCl = C_6H_5.CO.C_6H_5 + HCl.$$

(ii.) Homologues of both the reacting substances may be employed.

$$C_6H_6 + CH_3CH_2COCl = C_6H_5.CO.CH_2.CH_3 + HCl.$$
$$C_6H_6 + C_6H_5CH_2COCl = C_6H_5.CO.CH_2.C_6H_5 + HCl.$$
$$C_6H_5CH_3 + C_6H_5COCl = p\text{-}CH_3C_6H_4COC_6H_5 + HCl.$$

(A., 189, 84 ; B., 12, 2299.)

(iii.) The acid radical always enters the *para*-position to the alkyl radical ; if that is occupied, it goes to the *ortho*-. A little of the *ortho*-compound is formed along with the *para*- in all cases, so that in preparing, for instance, phenyl-*p*-tolyl-ketone, the method given in the last equation should not be used, but it should be made from benzene and *p*-toluoyl

chloride, when it is the only compound formed. (A., 189, 84; B., 12, 2299.)

$$C_6H_6 + p\text{-}CH_3C_6H_4COCl = p\text{-}CH_3C_6H_4COC_6H_5 + HCl.$$

The pure *o*- and *m*-compounds can be prepared in a similar manner.

(iv.) Instead of the hydrocarbons the phenol ethers which react with great ease can be employed; the same rules as to position apply.

$$C_6H_5.O.CH_3 + C_6H_5.CO.Cl = p\text{-}CH_3O.C_6H_4.COC_6H_5 + HCl.$$

(v.) Substituted acid chlorides may be used to obtain substituted ketones.

$$C_6H_6 + p\text{-}Br.C_6H_4.COCl = p\text{-}BrC_6H_4COC_6H_5 + HCl.$$
$$C_6H_6 + p\text{-}NO_2C_6H_4COCl = p\text{-}NO_2C_6H_4COC_6H_5 + HCl.$$

(vi.) The chlorides of the dibasic acids react in two ways: (*a*) With 1 mol. of hydrocarbon they give acid chlorides. (*b*) With 2 mols. of hydrocarbon di-ketones are formed, except in the case of phosgene.

$$COCl_2 + 2C_6H_6 = CO.(C_6H_5)_2 + 2HCl.$$

(B., 10, 1854.) See also E.P., 388734.

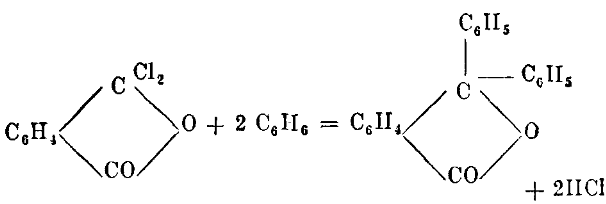
$$COCl_2 + 2C_6H_5CH_3 = CO.(C_6H_4.CH_3)_2[4:4'] + 2HCl.$$

(A., 312, 92; B., 7, 1183; 10, 2173; J. pr., [2], 35, 466.)

$$COCl_2 + C_6H_5N(CH_3)_2 = CO(C_6H_4N(CH_3)_2)_2[4:4'] + 2HCl.$$

(B., 19, 109; B., 24, 3198.)

The last compound 4 : 4′-tetramethyl-di-amino-benzophenone is also known as "Michler's ketone," and is an important intermediate in the preparation of dyestuffs of the fuchsine series, *e.g.*, crystal violet. For the preparation of this ketone by treatment of dimethylaniline with carbon dioxide in presence of aluminium chloride, see E.P., 353464.




With phthalyl chloride "diphenylphthalide," important on account of its relation to the fluorescein dyes, is formed (B., 14, 1865).

Comparing with Reaction XX. (*a*) it will be seen that phthalyl chloride is tautomeric. Succinyl chloride is also considered to be similarly tautomeric, a number of facts supporting this view. Unlike phthalyl chloride, however, it reacts in the symmetrical form.

(vii.) Naphthalene reacts in a manner similar to benzene,

$$C_{10}H_8 + C_6H_5COCl = \alpha\text{-}C_{10}H_7COC_6H_5 + HCl.$$

It will be noted in the following examples that the quantities of aluminium chloride used are larger than in the case of the hydrocarbons

synthesised by this reaction. This is necessary owing to the stability of the addition compounds of aluminium chloride with the product. So stable are those compounds that the aluminium chloride is unable to exert its catalytic action, and molecular quantities of the condensing agent have to be taken. (J. C. S., 83, 1470.)

PREPARATION 28.—**Acetophenone** (*Methyl phenyl ketone*).

$$C_6H_5.CO.CH_3. \qquad C_8H_8O. \qquad 120.$$

50 gms. (1 mol.) of freshly prepared finely powdered anhydrous aluminium chloride (see p. 506) are placed in a 500-c.c. flask attached to an upright condenser, 30 gms. (1 mol.) of dry benzene are immediately added, and then, while cooling the flask by ice-water, 35 gms. (excess) of acetyl chloride are slowly dropped in from a tap funnel fitted to the top of the condenser. A brown viscid mass is formed which, after standing for 1 hour, is poured on to ice and extracted with a little benzene. The extract is washed with dilute caustic soda and with water, dehydrated over calcium chloride, filtered and distilled. The fraction 190°—205° is redistilled.

$$C_6H_6 + CH_3COCl + AlCl_3 = C_6H_5COCH_3[AlCl_3] + HCl.$$
$$C_6H_5COCH_3[AlCl_3] + 3H_2O = C_6H_5COCH_3 + Al(OH)_3 + 3HCl.$$

*Yield.*—50% theoretical (22 gms.). Colourless plates; sweetish odour; insoluble in water; soluble in benzene; M.P. 20°; B.P. 202°; D. $^0_4$ 1·032. (A. Ch., [6], 1, 507; 14, 455.)

*Note.*—In all these experiments the aluminium chloride must be weighed out in a dry test tube closed by a cork.

PREPARATION 29.—**Benzophenone** (*Diphenyl ketone*).

$$C_6H_5.CO.C_6H_5. \qquad C_{13}H_{10}O. \qquad 182.$$

30 gms. (excess) of *dry* benzene, 30 gms. (1 mol.) of pure benzoyl chloride, and 130 gms. of *dry* carbon disulphide are placed in a dry flask and 29 gms. (1 mol.) of finely powdered, anhydrous aluminium chloride (p. 506) are added.

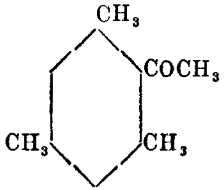
The flask is then connected with a long reflux condenser, and heated on a water bath kept at 50°, until only small amounts of hydrogen chloride are evolved (about 2½ hours). The carbon disulphide is then distilled off on a water bath (caution) and the still warm residue is carefully poured into a large flask containing 300 c.cs. of ice-water. The reaction flask is then washed out into the ice-water flask with 100 c.cs. of water, 10 c.cs. of conc. hydrochloric acid are added, and the whole steam distilled for 15 minutes. The cold residue is extracted with ether, the ethereal solution is repeatedly washed with water, filtered, and three times washed with dilute caustic soda solution. It is dehydrated over calcium chloride, filtered and distilled from a "high boiling point" distilling flask (see p. 19), the fraction 290°—305° being retained.

$$C_6H_6 + C_6H_5COCl + AlCl_3 = C_6H_5.CO.C_6H_5[AlCl_3] + HCl.$$
$$C_6H_5COC_6H_5[AlCl_3] + 3H_2O = C_6H_5.CO.C_6H_5 + Al(OH)_3 + 3HCl.$$

*Yield.*—80% theoretical (30 gms.). Colourless crystals; insoluble in water; soluble in benzene; M.P. 48°; B.P. $^{760}$ 307°; B.P. $^{12}$ 162°; a labile modification (M.P. 26°) also exists; it transforms to the stable modification on boiling or on touching with a little of the latter. (B., 26, R., 380; A. Ch., [6], 1, 518; Am. Soc., 50, 571; O.S., VIII., 26.)

The effect of carbon disulphide on the velocity of the action and on the yield should be noted by comparing the above preparation with the preceding.

PREPARATION 30.—**Acetylmesitylene** (1 : 3 : 5-*Trimethyl-2-acetyl-benzene*).



$C_{11}H_{14}O$ **162.**

25 gms. (1 mol.) of mesitylene (see p. 57), 75 gms. of carbon disulphide and 30 gms. (excess) of freshly distilled acetyl chloride are placed in a flask provided with a reflux condenser, and 33 gms. ($1\frac{1}{4}$ mols.) of finely powdered, freshly prepared, anhydrous aluminium chloride are added, gradually. The mixture is finally warmed for 15 minutes on a water bath and poured on to ice, 10 c.cs. of conc. hydrochloric acid are added, and the whole is steam distilled until no more oily drops pass over. The distillate is extracted with benzene and the extract washed with dilute caustic soda solution and with water, dried over calcium chloride and distilled, the fraction 230°—240° being retained.

$$C_6H_3(CH_3)_3[1:3:5] + CH_3.CO.Cl = C_6H_2(CH_3)_3(CO.CH_3)[1:3:5:2] + HCl.$$

*Yield.*—60% theoretical (20 gms.). Colourless liquid; B.P. 235°. (B., 24, 3542.)

PREPARATION 31.—4 : 4′-**Dimethylbenzophenone.**

$$[4]CH_3.C_6H_4.CO.C_6H_4CH_3[4']. \qquad C_{15}H_{14}O. \qquad 210.$$

This preparation must be conducted in a good draught cupboard.

100 gms. of toluene, containing 20% of carbonyl chloride (see p. 513) are placed in a flask to which is attached by a two-holed stopper a reflux condenser and a wide-stemmed glass filtering funnel. To the end of the condenser is attached a delivery tube leading to a fume duct. The flask is surrounded by a freezing mixture, and 50 gms. of finely powdered anhydrous aluminium chloride are gradually added through the funnel during 4 hours, the funnel being closed by a cork after each addition. When all has been added, the flask is very gently warmed for a short time, and the contents slowly poured into ice-water (caution). It is then steam distilled until nothing further passes over. The aqueous layer of the distillate is removed and a 1% solution of hydrochloric acid added to the solid matter, which is again steam distilled for about 30 minutes.

The solid matter in the distillate is filtered off, washed and recrystallised several times from dilute alcohol.

$$2C_6H_5CH_3 + COCl_2 \longrightarrow CO(C_6H_4.CH_3[4])_2 + 2HCl.$$

*Yield*.—50% theoretical (45 gms.). Colourless needles; insoluble in water; soluble in benzene and alcohol; M.P. 95°; B.P. 333°. (B., 10, 2173; A., 312, 92; J. pr., [2], 35, 466.)

*Note*.—Carbonyl chloride is extremely poisonous, and special care must be taken in its use.

**Reaction XX.** (*c*) **Action of a Mixture of Aluminium and Mercuric Chloride on a Mixture of an Aromatic Hydrocarbon and an Acyl Halide.** (J. C. S., 117, 1330.)—This modification of the Friedel-Crafts condensation has been fully dealt with under its application to the synthesis of hydrocarbons. In the case of ketones the results obtained are more in accordance with the results of the older method than were those discussed in the first hydrocarbon section.

PREPARATION 32.—**Acetophenone** (*Methyl phenyl ketone*).

$$C_6H_5.CO.CH_3. \qquad C_3H_8O. \qquad 120.$$

20 gms. (1 mol.) of *dry* benzene, and 20 gms. of mercuric chloride are placed in a flask fitted with a reflux condenser and 1 gm. of aluminium powder is added, gradually, and with vigorous shaking, the ensuing reaction being moderated by occasional cooling in an ice bath. A green, crystalline mass separates, and the reaction is completed by immersing the flask in tepid water for half an hour. The mercury liberated in the reaction is removed and the preparation of the catalyst is complete. 20 gms. (1 mol.) of acetyl chloride are added in small quantities through the condenser, the reaction mixture being well agitated by a mechanical stirrer. (For a suitable apparatus, see Fig. 38.) The whole is allowed to stand for 2 hours, and then heated to 40° for 1 hour. On cooling, water is added to decompose the product, and the liberated oil extracted with benzene. The extract is dried over calcium chloride and fractionated, the fraction 195°—205° being retained.

$$C_6H_6 + Al + 2HgCl_2 = C_6H_6.AlCl_3.HgCl + Hg.$$
$$C_6H_6.AlCl_3.HgCl + CH_3COCl = CH_3.CO.C_6H_5.AlCl_3.HgCl + HCl.$$
$$2CH_3COC_6H_5.AlCl_3.HgCl + 6H_2O = 2CH_3COC_6H_5 + 2Al(OH)_3 + Hg_2Cl_2 + 6HCl.$$

*Yield*.—60% theoretical (18 gms.). Colourless plates; sweetish odour; soluble in benzene; insoluble in water; M.P. 20°; B.P. 202°; D. $^0_4$ 1·032. (J. C. S., 117, 1330.)

This yield of acetophenone is 10% better than that obtained in the ordinary Friedel-Crafts reaction. A similar method can be applied to the preparation of *p*-tolyl-methyl-ketone, 20 gms. (1 mol.) of dry toluene, 2 gms. of aluminium powder, 35 gms. of mercuric chloride, and 17 gms. (1 mol.) of acetyl chloride being used. The yield is 45% theoretical (13 gms.). The ketone is obtained as a low-melting solid, B.P. 224°.

**Reaction XX.** (*d*) **Combined Action of Carbon Monoxide and Hydrogen Chloride on an Aromatic Hydrocarbon in presence of a Mixture of Anhy-**

**drous Aluminium and Cuprous Chlorides** (Gattermann-Koch). (B., 30, 1622; A., 347, 347; 357, 313.)—Since a mixture of carbon monoxide and hydrogen chloride behaves as the unknown formyl chloride, it is possible to utilise the Friedel-Crafts method in the synthesis of aldehydes. The isolation and use of the addition compound $CO.HCl.AlCl_3$ are described in E.P., 445554.

$$HCl + CO[Cu_2Cl_2] = H.CO.Cl.[Cu_2Cl_2].$$
$$CH_3.C_6H_5 + H.CO.Cl[AlCl_3] = CH_3.C_6H_4.CHO.[Al.Cl_3] + HCl.$$
$$CH_3.C_6H_4.CHO.[AlCl_3] + 3H_2O = CH_3.C_6H_4.CHO + Al(OH)_3 + 3HCl.$$

Benzene itself does not react—unless hydrobromic acid is used—and can on that account be used as a solvent (D.R.P., 126421).

Many other hydrocarbons, *o*- and *m*-xylene, mesitylene, ethylbenzene, diphenyl, etc., can all be employed to give the corresponding aldehydes. The CHO group enters the *para*-position to the alkyl residue just as in the ketonic synthesis. Thus *o*-xylene gives 3 : 4-di-methyl-benzaldehyde.

Since the Friedel-Crafts reaction when applied to the phenol ethers yields the corresponding ketones far more easily than the same reaction applied to hydrocarbons (see Reaction XX. (*b*) (iv.)), it is noteworthy that the above reaction does not apply to the phenol ethers. To obtain aldehydes from them or from phenols, a modified method must be used (see pp. 104, 106).

PREPARATION 33.—***p*-Tolylaldehyde** (1 : 4-*Methylbenzaldehyde*).

$CH_3.C_6H_4.CHO[1:4]$. $C_8H_8O$. 120.

To 30 gms. (1 mol.) of freshly distilled toluene (B.P. 110°) contained in a wide-necked vessel cooled with water, 45 gms. of pulverised freshly prepared aluminium chloride and 5 gms. of pure cuprous chloride are added. The vessel is closed by a three-holed cork, in the middle hole of which is inserted a glass tube which carries an efficient stirrer; the other holes are used for the inlet and outlet tubes. After the apparatus has been firmly fastened in a clamp, it is immersed in a jar filled with water at 20°. A current, not too rapid, of carbon monoxide and hydrogen chloride is led in through a prong-shaped tube while the stirrer is set in motion. The gases are dried by bubbling each through conc. sulphuric acid, their rates of entry being so regulated that the volume of carbon monoxide is about twice that of the hydrogen chloride passing in. The escaping gas is led directly to the hood opening of a draught chamber. In the course of an hour, when about 1—2 litres of carbon monoxide have been passed into the mixture, the temperature rises to 25°—30°; the remainder of the gas is passed in during 4—5 hours. Should the reaction mixture become so viscous before the lapse of this time that the stirrer revolves only with difficulty, the reaction may be stopped. The viscid product is then poured into a large flask containing crushed ice; the aldehyde formed and any unattacked toluene are distilled over with steam. The distillate —oil and water—is then shaken up with a sodium bisulphite solution (see p. 510) for a long time, and the toluene which does not dissolve is separated in a funnel. If the aldehyde-bisulphite compound should

crystallise out, water is added till it dissolves. The filtered aqueous solution is then treated with anhydrous sodium carbonate until it shows a decided alkaline reaction, the aldehyde distilled off in steam, extracted with ether, the extract dried over anhydrous calcium chloride, and the ether removed on a water bath.

$$CH_3.C_6H_4.H + Cl.CO.H = CH_3.C_6H_4.CHO + HCl.$$

*Yield.*—60% theoretical (22 gms.). Colourless liquid; B.P. 204°. (B., 31, 1149; A., 347, 347; J. C. S., 1932, 2793; O.S., XII., 80.)

**Reaction XX.** (*e*) **Action of Aliphatic or Aromatic Carboxylic Acids or their Chlorides or Anhydrides on Phenolic Compounds in presence of Zinc Chloride to yield Phenolic Ketones** (Nencki).

$$R.COOH + C_6H_{(6-x)}(OH)_x \longrightarrow R.CO.C_6H_{(5-x)}(OH)_x + H_2O.$$

Thus acetic and higher fatty acids combine with resorcinol (U.S.P., 219,922 (1923)); propionyl chloride with phenol (J. C. S., 55, 546); fatty acids with pyrogallol, hydroquinone or α-naphthol (J. pr., 23, 546; 43, 86); benzoic acid with pyrogallol (D.R.P., 49149 (1889)). See also B., 63 (B), 2740; and O.S., XIV., 40.

The reaction is also of importance as a first stage in the preparation of certain higher phenols (p. 177).

PREPARATION 34.—**Resacetophenone** (1-*acetyl*-2 : 4-*dihydroxybenzene*).

$$CH_3CO.C_6H_3(OH)_2. \qquad C_8H_8O_3. \qquad 152.$$

30 gms. of fused zinc chloride are dissolved in 30 gms. of hot glacial acetic acid and 20 gms. of resorcinol added. Heating is continued in an open flask on a sand bath until (about 145°—150°) the liquid begins to boil vigorously, when the flame is removed, and the reaction left to complete itself on the hot sand bath. The temperature should not exceed 150°, nor should it remain at 150° for too long a time as resinous by-products are thus formed—indicated by the reaction mixture becoming deep red. After cooling, the product is thoroughly mixed with 200 c.cs. of 2% aqueous hydrochloric acid to dissolve the zinc chloride, and the undissolved portion collected by filtration. This dark brown lustrous product is dissolved in caustic soda solution, boiled with decolourising carbon and filtered. As resacetophenone is difficultly soluble in water it is precipitated from the filtrate by acidification with hydrochloric acid. It may, if necessary, be purified by a repetition of this treatment or by recrystallisation from 2% hydrochloric acid.

$$CH_3COOH + C_6H_4(OH)_2 \longrightarrow C_6H_3(OH)_2.COCH_3 + H_2O.$$

*Yield.*—40% theoretical (11 gms.). Needles, M.P. 142°. Decomposes on distillation even at reduced pressure. (See also O.S., XIV., 40.)

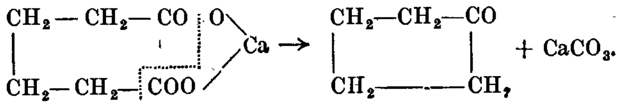
**Reaction XXI.** (*a*) **Dry Distillation of the Barium or Calcium Salt of a Fatty Acid with Barium or Calcium Formate.**—This is one of the methods by which aldehydes may be obtained from acids. Like most dry distillations, the yields are poor, and the method is seldom used.

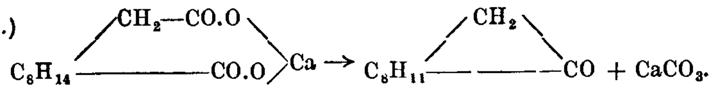
$$\begin{array}{l:l:l} CH_3— & CO.O.Ca.O. & CO—CH_3 \\ H.CO. & O.Ca.O.CO & H \end{array} = 2CH_3.CHO + 2CaCO_3.$$

**Reaction XXI.** (*b*) **Dry Distillation of the Barium or Calcium Salts of Fatty Acids.** (Z. Ch., 19, 1755.)—This is an old method of preparing ketones, and is still used. Originally calcium salts were employed, but barium salts have been found to give better yields. Mixed ketones can be prepared by distilling an intimate mixture of the salts of two acids, but the symmetrical ketones from the single acids are also formed at the same time. The method is perfectly analogous to that given above for aldehydes. Almost all of the fatty acids give this reaction, but it is better to distil under reduced pressure when working with the higher members of the series. If the salt of a dibasic acid be used, since the two carboxyls are already linked together, distillation produces a ring compound. This is a very important method of ring-formation, and serves for a very large variety of compounds. The following examples will give an idea of the scope of the reaction—

(i.) $$\begin{array}{r|c|l} CH_3.CO. & O.Ca.O.CO. & CH_3 \\ & + & \\ C_6H_5. & CO.O.Ca.O. & CO.C_6H_5. \end{array} \rightarrow 2CH_3.CO.C_6H_5 + 2CaCO_3.$$

Some $(CH_3)_2CO$ and $(C_6H_5)_2CO$ are also formed.

(ii.) 

(iii.) 

(iii.) represents the last step in the synthesis of camphor by heating calcium homo-camphorate in a current of carbon dioxide (Z. Ch., 19, 1755).

Cyclic ketones containing up to 34 C-atoms in the ring have been prepared from the corresponding dicarboxylic acids. By the Clemmensen reduction (Reaction LVIII. (*c*)) the ketones have been converted into cyclic hydrocarbons. These large ring compounds are remarkably stable. (H. Acta, 11, 496, 670; 13, 1152; 17, 78.)

PREPARATION 35.—**Acetone** (*Dimethyl ketone*).

$$CH_3COCH_3. \qquad C_3H_6O. \qquad 58.$$

100 gms. (2 mols.) of anhydrous calcium or barium acetate are distilled from a metal retort attached to a long condenser, some dry iron turnings being previously mixed with the salt to distribute the heat. When no more liquid distils, the distillate is shaken for 5 hours with three volumes of saturated sodium bisulphite solution (see p. 510). The crystalline compound is filtered off, dissolved in the minimum quantity of water. Anhydrous sodium carbonate is added until the solution is alkaline, and the acetone then distilled from a water bath. The distillate is dried over calcium chloride and redistilled, the fraction 55°—59° being retained.

$$\begin{array}{r|c|l} CH_3CO & O\ Ca\ O.\ OC & CH_3 \\ CH_3 & CO\ .\ O\ Ca\ O & OC.CH_3 \end{array} \rightarrow 2CH_3COCH_3 + 2CaCO_3.$$

*Yield.*—20% theoretical (12 gms.) from calcium acetate; 25% theoretical (10 gms.) from barium acetate. Colourless mobile liquid; B.P. 56·3°; D. $^{15}_{4}$ 0·742; soluble in water. (E.P., 392652.)

The distillate may also be purified by adding an equal volume of water to dissolve the acetone, dehydrating for several hours over quicklime under a reflux, distilling, and dehydrating further over calcium chloride.

For dehydration with anhydrous calcium nitrate, see Ann. Chim. App., 1935, 657.

PREPARATION 36.—**Benzophenone** (*Diphenyl ketone*).

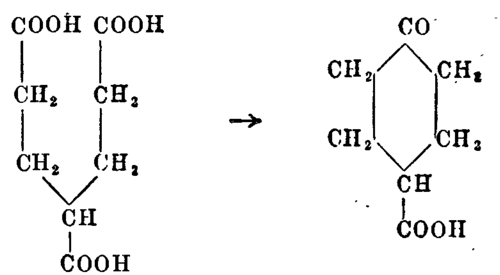
$C_6H_5.CO.C_6H_5$. $C_{13}H_{10}O$. 182.

10 gms. (2 mols.) of benzoic acid are heated to boiling with 25 gms. (excess) of slaked lime and ten times the weight of water, until the acid is completely dissolved and the liquid reacts alkaline. It is then filtered hot from the excess of slaked lime. On cooling most of the calcium benzoate separates out from the filtrate in white needles. The remainder is obtained on evaporating the mother liquor. The salt is filtered as well as possible at the pump, pressed in cloth (p. 33) and completely dried in metal dishes over a free flame.

The mass is now introduced into a metal retort (made of iron or copper), which is connected with a long condenser tube. The retort must not be filled more than two-thirds full. It is heated over a powerful gas burner, so that the dry distillation of the salt proceeds as quickly as possible. A pale brownish coloured mixture of benzene, benzophenone and aromatic products first distils over. The distillation is stopped when the distillate becomes brown and viscous. The distillate is dried with calcium chloride, and then fractionated. The fraction 250°—310° contains the benzophenone. The product sometimes solidifies quickly, but more frequently remains syrupy for days. Crystallisation begins, however, at once, when a small quantity of solid benzophenone is added. The crystals are freed from the oily mother liquor by pressing between filter paper, or by spreading on a porous tile, and are recrystallised from ligroin.

*Yield.*—30% theoretical (2 gms.) (see p. 87).

**Reaction XXI. (*c*) Action of Acetic Anhydride on Carboxylic Acids and subsequent Distillation.**—This method of preparing ketones is worthy of note because it was used to obtain δ-ketohexahydrobenzoic acid from δ-carboxypimelic acid.



δ-Ketohexahydrobenzoic acid is important, because it is the starting point in one of the methods of synthesising terpenes (see p. 73).

**Reaction XXI.** (*d*) **Catalytic Action of its Manganese Salt on the Vapour of a Fatty Acid.**—When acetic acid vapour is passed over heated manganese acetate, acetone is formed. The process is continuous and the method gives better yields than the older distillation method. The cycle of changes which takes place in the action may be formulated somewhat as follows—

$$Mn.(O.OC.CH_3)_2 = (CH_3)_2CO + MnCO_3.$$
$$MnCO_3 + 2CH_3COOH = Mn.(O.OC.CH_3)_2 + CO_2 + H_2O.$$

The principle of this method has been utilised on the industrial scale, and with success for the preparation of acetone. The acetic acid may be prepared from acetylene *viâ* acetaldehyde (see p. 433), thus providing a commercial synthesis of acetone from coke.

PREPARATION 37.—**Acetone** (*Propanon*).

$$CH_3.CO.CH_3. \qquad C_3H_6O. \qquad 58.$$

About 20 gms. of manganous carbonate are made into a thick paste with water in a basin. This is stirred with an equal bulk of pumice in small pieces, and then placed in an air oven at 110°—120° until quite dry. When dry it is loosely packed into a combustion tube, sufficient being taken to fill rather more than half (40 cms.) the length of the tube ; two asbestos plugs are used to keep the layer in position.

The combustion tube is then placed in a long cylindrical air bath (see Fig. 44). The side tube of a distilling flask containing acetic acid is inserted through an ordinary cork in one end of the combustion tube. The other end of the combustion tube may be bent and drawn out after the fashion of an adapter, or it may be fitted with a cork and delivery tube ; in either case it is connected to an apparatus for condensing the mixture of acetone and acetic acid which passes over (see p. 50 for condenser arrangement). The air bath is heated to 120°—130° and maintained at this while the combustion tube is filled with the vapour of acetic acid by boiling the acetic acid in the distilling flask for a few minutes. The air bath is then raised to 400°—450°, *i.e.*, until the bottom of the air bath is at a good red heat (*N.B.*, a thermometer should not be used unless it is nitrogen filled). Shields of thick asbestos paper should be placed over the air bath to conserve heat. The distillate which collects in the receivers (the second receiver should be cooled in ice) consists of acetic acid, acetone and water. If this distillate is passed a second or third time over the catalyst, the yield of acetone is increased. In this way excellent yields may be obtained. The final distillate is distilled from an apparatus on a water bath, using a thermometer and efficient condenser, collecting what distils up to 80° ; this is dried in contact with solid potassium carbonate and fractionally distilled.

$$CH_3COOH + HOOC.CH_3 = CH_3.CO.CH_3 + CO_2 + H_2O.$$

(See p. 92.) (E.P., 392652. See also J. Eng., 26, 388, 1014.)

**Reaction XXII.** (*a*) **Action of Magnesium Alkyl or Aryl Halide on (i.) excess of Ethyl Formate, (ii.) Ethyl Orthoformate, (iii.) di-substituted**

**Formamide and other Derivatives of Formic Acid** (Grignard).—This is the Grignard method of preparing aldehydes. The same remarks apply to this reaction as to the other "Grignards" dealt with. The equations illustrate its course.

(i.) $$H.COOC_2H_5 + C_6H_5MgI \rightarrow C_6H_5CHO + C_2H_5O.Mg.I.$$

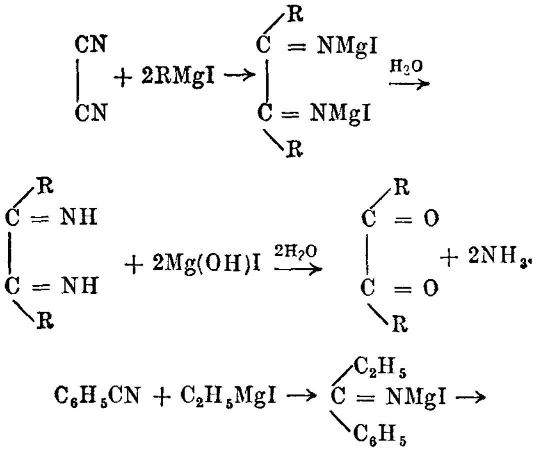
(ii.) $$H.C(OC_2H_5)_3 + C_6H_5MgI + H_2O. \rightarrow C_6H_5CHO + C_3H_5OMgI + 2C_2H_5OH.$$

(iii.) $$H.CO.N(CH_3)_2 + C_6H_5MgI \rightarrow HC(C_6H_5)(OMgI)N(CH_3)_2 \rightarrow C_6H_5CHO + (CH_3)_2NH + Mg(OH)I.$$

The course of the above reaction should be studied carefully, as it is somewhat different from those so far discussed.

**Reaction XXII.** (*b*) **Action of Magnesium Alkyl or Aryl Halide on (i.) Nitriles, and (ii.) Amides** (Grignard).—This is the analogous reaction to the foregoing, ketones being obtained in place of aldehydes by using derivatives of acids other than formic. The esters, however, do not figure among the derivatives which can be employed (see p. 75).

**(i.)**



$$C_6H_5.CO.C_2H_5 + NH_3 + Mg(OH)I.$$

**(ii.)** $$C_6H_5CONH_2 + CH_3MgI \rightarrow C_6H_5C(CH_3)(OMgI)NH_2 \rightarrow C_6H_5.CO.CH_3 + Mg(OH)I + NH_3.$$

**Reaction XXII.** (*c*) **Action of Zinc Alkyl on Acyl Chlorides in certain proportions.**—The preparation of alcohols by this method has already been discussed (Reaction XV.). By using only 1 mol. of zinc alkyl to 2 mols. of acid chloride, the reaction can be stopped at the intermediate ketone stage. In the Grignard reaction with acid chlorides, it has not been found possible to do this owing to the greater reactivity of the Grignard compounds.

$$2CH_3.CO.Cl + Zn(CH_3)_2 = 2CH_3COCH_3 + ZnCl_2.$$

**Reaction XXIII.** (*a*) **Condensation of Ethyl Formate with certain Keto-Compounds under the influence of Sodium Ethoxide** (Claisen). (A., 283,

306.)—This condensation is undergone by all compounds containing the group—$CH_2$—CO—. It follows the same lines as the other ester-ketone condensations (see pp. 142 *et seq.*).

$$\underset{\displaystyle R.CH_2}{\overset{COR}{|}} + C_2H_5O.O.C.H \rightarrow \underset{\displaystyle R.CH.CHO}{\overset{COR}{|}} + C_2H_5OH$$

$$\rightarrow \underset{\displaystyle R.C : CH(OH)}{\overset{COR}{|}} + C_2H_5OH.$$

The compounds so formed were at first thought to be aldehyde derivatives, thus the compound derived from acetophenone was thought to have the formula—$C_6H_5.CO.CH_2.CHO$. Support was lent to this view by the fact that the compound gave an oxime, $C_6H_5.CO.CH_2.CH : NOH$. On the other hand, in many reactions it behaved as if it had the formula $C_6H_5$. CO.CH : CH(OH). It gave a sodium salt, being obtained as such in its preparation; and a chloro compound, $C_6H_5.CO.CH : CHCl$, when treated with $PCl_5$. The view now held is that these "hydroxymethylene" compounds are tautomeric; both keto and enol forms being present. The enol form is of special interest on account of the great reactivity of the hydroxyl group. The double bond seems to have the same activating effect as the keto group in carboxyl compounds, the hydroxyl group behaving more like an acid hydroxyl than an alcoholic. The chloride derived from it is nearly as reactive as an acid chloride; and the corresponding amino compound behaves rather as an amide than as an amine.

The compounds separate from the condensation as sodium salts. From the simple ketones, the compound formed is not stable and undergoes change on precipitation from its sodium salt. The formation of a hydroxymethylene compound is used as proof of the presence of the group—$CH_2$—CO—in camphor. The following preparation shows the details of the method.

PREPARATION 38.—**Camphoraldehyde** (*Hydroxymethylenecamphor*).

$$C_8H_{14}\left\langle\begin{array}{l} CO \\ | \\ CH.CHO \end{array}\right. \text{ and } C_8H_{14}\left\langle\begin{array}{l} CO \\ | \\ C = CH(OH). \end{array}\right. \qquad C_{11}H_{16}O_2. \qquad 180.$$

90 gms. (excess) of camphor are dissolved in toluene which has been freed from water by standing over calcium chloride, and to this solution are added 6 gms. of sodium wire. To the well-cooled mixture 19 gms. (1 mol.) ethyl formate are added, when it is set aside in an ice chest for 24 hours. It is then poured into ice-water, and after vigorous shaking the aqueous layer removed. After acidifying with acetic acid, and then extracting with ether, the ethereal extract is dried over calcium chloride. The ether is removed by distillation, and the residue, after being placed in a basin, is allowed to evaporate slowly at ordinary temperature. The oil

which remains solidifies on standing to colourless crystals. These may be purified by steam distillation and crystallisation from dilute acetic acid.

$$C_8H_{14}\left\langle\begin{array}{l}CO\\ |\\ CH_2\end{array}\right. + C_2H_5ONa + H.COOC_2H_5 \rightarrow C_8H_{14}\left\langle\begin{array}{l}CO\\ |\\ C = CH(ONa)\end{array}\right. + 2C_2H_5OH$$

*Yield.*—Theoretical (46 gms.). Soluble in ether; M.P. 80°—81°. (A., 283, 306.)

**Reaction XXIII.** (*b*) **Condensation of Esters other than Ethyl Formate, with certain Ketones under the influence of Sodium Ethylate, Metallic Sodium, or Sodamide** (Claisen). (B., 22, 1009; 23, R., 40; 38, 695.)—This is a similar reaction to that discussed above, and is part of a general condensation undergone by esters with oxy compounds, other phases of which are discussed on pp. 142–150.

The reaction may be formulated as follows—

$$R_1COOEt + H_2.CR_{11}COCR_{111} = R_1.CO.CR_{11}COCR_{111} + Et.OH.$$

where R may be hydrogen or an alkyl or aryl group. It is only these ketones which possess the group $\overset{|}{\underset{|}{HC}}$—CO—that undergo the reaction. The compounds formed are always 1 : 3-di-ketones. The way in which the condensing agent brings about the condensation is described under the actual preparations (see Preparation 39). The compounds themselves are di-ketones, but their sodium salts are derived from the corresponding enol compounds (B., 25, 3074). Of the three condensing agents, sodamide is the most and sodium ethylate the least effective.

Preparation 39.—**Benzoylacetone** (1-*Phenyl*-1 : 3-*butandione*).—

$$C_6H_5.CO.CH_2.CO.CH_3. \qquad C_{10}H_{10}O_2. \qquad 162.$$

*Method I.*—6 gms. (1 mol.) of fresh dry sodium ethylate (see p. 509) are added to 20 gms. (excess) of *dry* ethyl acetate under cooling by water. After 15 minutes, 10 gms. (1 mol.) of acetophenone are added; the separation of the sodium salt of benzoyl acetone immediately begins. A little *dry* ether is added, and in 4 hours the sodium compound is filtered off, washed with ether, air-dried, dissolved in cold water, and the solution acidified with acetic acid. Benzoyl acetone separates.

$$(1)\ CH_3COOEt + C_2H_5ONa = CH_3C\left\langle\begin{array}{l}ONa\\ OC_2H_5\\ OC_2H_5.\end{array}\right.$$

$$(2)\ CH_3C\left\langle\begin{array}{l}ONa\\ OC_2H_5\\ OC_2H_5\end{array}\right. + CH_3COC_6H_5$$

$$= CH_3C(ONa) : CH.CO.C_6H_5. + 2C_2H_5OH.$$

$$CH_3C(ONa) : CH.CO.C_6H_5 + CH_3.COOH$$

$$= CH_3CO.CH_2CO.C_6H_5 + CH_3COO.Na.$$

*Yield.*—66% theoretical (10 gms.). Colourless crystals; insoluble in water; M.P. 61°; gives a deep violet coloration with ferric chloride and a bluish-green crystalline precipitate of copper benzoyl acetone with alcoholic copper acetate. This shows the compound to be tautomeric, a little of the enol form being present at ordinary temperatures. The acidity of the hydroxyl group in the enol form is not so marked as it is in the case of the hydroxymethylene compounds; nevertheless, the metallic salts of benzoyl acetone and such di-ketones are remarkably stable, and on account of their great crystallising power have been used for the determination of the valency and atomic weight of the rare elements. They are also of importance in the modern theory of co-ordination. (C., 1900, I., 588; B., 34, 2584.)

*Method II.*—25 gms. (excess) of ethyl acetate and 30 gms. of acetophenone (1 mol.) are dissolved in 200 c.cs. of anhydrous ether. To this is slowly added with gentle cooling 20 gms. (excess) of powdered sodamide. It is then set aside for 24 hours, when the sodium salt separates, and is poured on to a mixture of ice and water sufficient to dissolve it completely. The aqueous layer is separated, and the ether removed from it by passing air through. Acetic acid is then added until the solution is acid, the precipitated benzoylacetone being filtered off and washed with water.

$$CH_3COOC_2H_5 + NaNH_2 \rightarrow CH_3C\begin{matrix} / ONa \\ - OC_2H_5. \\ \backslash NH_2 \end{matrix}$$

$$CH_3C\begin{matrix} / ONa \\ - OC_2H_5 \\ \backslash NH_2 \end{matrix} + CH_3COC_6H_5 \rightarrow \begin{matrix} CH_3C(ONa) : CH.COC_6H_5 \\ + C_2H_5OH + NH_3. \end{matrix}$$

$$CH_3C(ONa) : CH.COC_6H_5 + CH_3COOH \rightarrow \begin{matrix} CH_3C(OH) : CH.COC_6H_5 \\ + CH_3COONa. \end{matrix}$$

$$CH_3C(OH) : CHCOC_6H_5 \rightleftarrows CH_3COCH_2COC_6H_5.$$

*Yield.*—75% theoretical (30 gms.). Colourless crystals; M.P. 61°; insoluble in water. (B., 36, 695.)

Thus the yield is improved by using ether as a solvent, and by replacing sodium ethylate by sodamide.

**Reaction XXIV. Condensation of certain Carbonyl Compounds with one another under the influence of Dehydrating Agents.** (A., 223, 139.)—Aldehydes and ketones readily condense with one another under the influence of such reagents as zinc chloride, hydrochloric acid, sulphuric acid, alkali hydroxides, sodium acetate solution, etc., to give $\alpha\beta$-olefinic aldehydes and ketones:

The reaction may be divided into the following:—

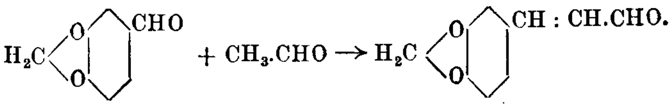
(i.) Two molecules of the same or different aldehydes condense to give an olefinic aldehyde. Acetaldehyde by treatment with zinc chloride yields crotonaldehyde. (B., 14, 514; 25, R., 372.)

$$CH_3CHO + CH_3CHO \rightarrow CH_3CH(OH)CH_2CHO \rightarrow CH_3CH = CHCHO.$$

By using condensing agents which are not at the same time dehydrating agents, the intermediate aldol compound can be isolated (see p. 101). A mixture of acetaldehyde and benzaldehyde yields cinnamic aldehyde by the action of hydrogen chloride, sodium hydrate, or sodium ethylate. (B., 17, 2117; 20, 657.)

$$C_6H_5CHO + CH_3CHO \longrightarrow C_6H_5CH = CHCHO + H_2O.$$

Piperonyl acrolein is obtained from piperonal and acetaldehyde. This is the initial step in the synthesis of piperine, one of the first alkaloids synthesised. (B., 27, 2958.)



(ii.) An aldehyde and a ketone or two ketones condense to yield an olefinic ketone.

Citral and acetone give pseudo-ionone. (B., 27, R., 768; see Reaction XVIII. (iv.).)

$$(CH_3)_2C : CHCH_2CH_2C(CH_2) : CHCHO + CH_3COCH_3$$
$$\longrightarrow (CH_3)_2C : CHCH_2CH_2C(CH_3) : CHCH : CHCOCH_3.$$

Acetone yields mesityl oxide. (A., 178, 351; B., 59, 2188.)

$$CH_3.CO.CH_3 + CH_3.CO.CH_3 \longrightarrow (CH_3)_2C : CHCOCH_3.$$

Hydrochloric acid is best suited for this condensation, the acetone being saturated with it in the cold.

(iii.) Several molecules of the same ketone may condense to yield di- and poly-olefinic ketones. (B., 36, 2555; C., 1903, II., 566.) Three molecules of acetone form phorone. (See also C. r., 190, 1349.)

$$3CH_3COCH_3 \longrightarrow (CH_3)_2C = CH.CO.CH = C(CH_3)_2.$$

PREPARATION 40.—**Styryl Methyl Ketone** (*Benzylideneacetone*).

$$C_6H_5CH : CH.CO.CH_3. \qquad C_{10}H_{10}O. \qquad 146.$$

2 gms. (1 mol.) of benzaldehyde and 3·5 gms. (excess) of acetone are heated with 20 c.cs. of 10% caustic soda solution on a water bath for 1 hour. The crystals which separate on cooling are filtered off and recrystallised from a little alcohol.

$$C_6H_5.CHO + CH_3.CO.CH_3 = C_6H_5CH : CH.CO.CH_3 + H_2O.$$

*Yield.*—Theoretical (3 gms.). Colourless crystals; dissolve with an orange-red colour in sulphuric acid; M.P. 42°; B.P. 262°. (A., 223, 139; B., 6, 254.)

*o*- and *p*-nitrobenzylidene acetones can be prepared in the same way from *o*- and *p*-nitrobenzaldehydes respectively. They melt at 60° and 110°.

PREPARATION 41.—**Phenyl Styryl Ketone** (*Benzylideneacetophenone*).

$$C_6H_5.CH : CH.CO.C_6H_5. \qquad C_{15}H_{12}O. \qquad 208.$$

2·1 gms. (1 mol.) of benzaldehyde and 2·4 gms. (1 mol.) of acetophenone are dissolved in 20 gms. of alcohol, 2 gms. of 10% caustic soda solution are added, and the whole allowed to stand for 24 hours. The precipitate is recrystallised from ligroin.

$$C_6H_5CHO + CH_3COC_6H_5 = C_6H_5CH : CH.CO.C_6H_5 + H_2O.$$

*Yield.*—Theoretical (4 gms.). Colourless crystals; M.P. 57°—58°; B.P. 346°. (B., 20, 657.)

**Reaction XXV. Action of an Alkyl Halide on the Sodio-derivative of certain Ketones.** (B., 21, 1297; 23, 2072.)—The fact that two phenyl groups have something of the same acidifying influence as one carbonyl group is shown in the case of desoxybenzoin, $C_6H_5.CO.CH_2C_6H_5$; one of the two methylene hydrogens in this compound is replaceable by sodium, and with the sodium compound the same kind of synthesis may be effected as with sodio aceto-acetic ester. The methylene group behaves as if it were between two carbonyl groups, except that the second methylene hydrogen is not replaceable.

$$C_6H_5.CO.CH_2C_6H_5 \xrightarrow{Na} C_6H_5.C(ONa) : CHC_6H_5$$

$$\xrightarrow{C_2H_5I} C_6H_5.CO.CH(C_2H_5)C_6H_5.$$

Desoxytoluoin $CH_3.C_6H_4.CH_2.CO.C_6H_4.CH_3$ and desoxyanisoin $CH_3O.C_6H_4.CH_2CO.C_6H_4OCH_3$ behave similarly, as do all the phenylbenzyl ketones.

# CHAPTER VI

## CARBON TO CARBON

### Hydroxy-Oxy Compounds

The reactions below are those in which carbon atoms are linked together to give compounds containing both a hydroxyl and an oxy (carbonyl) group. In the aliphatic series there are three main divisions of such compounds :—

(*a*) The carbonyl group is linked to a terminal carbon, and the hydroxyl group to another carbon—aldols.

(*b*) The carbonyl group is linked to a non-terminal carbon, and the hydroxyl group to another—ketols.

(*c*) The carbonyl group is linked to the same carbon (necessarily terminal) as the hydroxyl group—acids.

The above only applies to the simplest hydroxy-oxy compounds ; acid-ketols, ketaldols, and acid ketaldols also exist.

The terms aldol and ketol are not usually applied in the aromatic series, but there is no reason why salicylaldehyde, for instance, should not be termed an aldol—or an aldphenol, if it is desired to restrict " ol " to purely alcoholic hydroxyls.

**Reaction XXVI.** (*a*) **Condensing Action of Potassium Cyanide, Potassium Carbonate, or other substances on Aliphatic** (Claisen) **and Aromatic Aldehydes** (Liebig). (J. C. S., 117, 324.)—With aliphatic and aromatic aldehydes this condensation follows very different lines. In the former the condensation takes place between the aldehydic carbon of one molecule and the α-carbon of another molecule. The same or different aldehydes may be used.

$$2R_1RCH.CHO = RR_1CH.CH(OH).C(RR_1).CHO.$$
$$R.CH_2.CHO + R_1CHO = R_1CH(OH).CH(R.)CHO.$$

It will be seen that only an aldehyde with at least one α-hydrogen can condense with itself or with another aldehyde. This latter, however, need have no particular structure. Condensing agents stronger than those mentioned above eliminate water if possible, after condensation. Two α-hydrogen atoms in an aldehyde are necessary for this change (see Reaction XXIV.).

It is worth noting that if the aldol condensation takes place in the presence of magnesium amalgam, the aldehydic group is simultaneously reduced and a 1 : 3-dihydric alcohol is formed.

When aromatic aldehydes are heated with potassium cyanide in aqueous alcoholic solution, the aldehyde groups condense and a ketol is formed. The reaction was discovered by Liebig for benzaldehyde (A., 3, 276), but

was later applied to other aromatic aldehydes (B., 25, 293; 26, 60), and since then some heterocyclic aldehydes have been found to undergo the reaction. (B., 28, R., 992.)

Theoretically the reaction is supposed to take place according to the following equations—

$$C_6H_5.CHO + KCN + H_2O \longrightarrow \underset{\text{Cyanohydrin.}}{C_6H_5CH(OH)CN} + KOH.$$

$$C_6H_5C\begin{cases} OH \\ -H \\ CN \end{cases} + C_6H_5CHO \longrightarrow \underset{\text{Aldol condensate.}}{C_6H_5C(OH)CN - CH(OH)C_6H_5}$$

$$\longrightarrow \underset{\text{Benzoin.}}{C_6H_5.CO.CH(OH)C_6H_5} + HCN.$$

The action of the potassium cyanide is catalytic, a small quantity being capable of condensing a large quantity of aldehyde.

For the preparation of aliphatic acyloins from esters, see O.S., XIII., 24.

PREPARATION 42.—**Aldol** (*β-Hydroxybutaldehyde*).

$$CH_3.CHOH.CH_2.CHO. \qquad C_4H_8O_2. \qquad 88.$$

200 c.cs. of ice-cold water are placed in the apparatus (Fig. 50) which is immersed in a cooling bath. 100 gms. of freshly distilled acetaldehyde, in portions at a time, are introduced while the cork is momentarily withdrawn, the bottle being agitated slightly during the addition, and great care being taken that the temperature of the contents does not rise above 0°. A suitable cooling bath for this stage consists of ice, water and a little hydrochloric acid. When all the aldehyde is added, the cooling bath is replaced by one of ice and hydrochloric acid, and when the temperature of the contents of the bottle has fallen to − 12°, 100 c.cs. of a 2·5% solution of potassium cyanide are slowly dropped in while the bottle is rotated; the temperature must be kept below − 8°. After the cyanide is added, the mixture is kept for 2 hours below − 8°, the freezing mixture being renewed if necessary, and then for 30 hours in an ice chest at 0°. The resulting syrupy solution of pale yellow colour is saturated in the cold with common salt, and then quickly extracted four times with a moderately large volume of ether. The ethereal extracts are dried over anhydrous sodium sulphate, the ether distilled off, and the residue distilled under reduced pressure. Aldol passes over at 80°—90° and 20 mms. pressure. A suction flask contain-

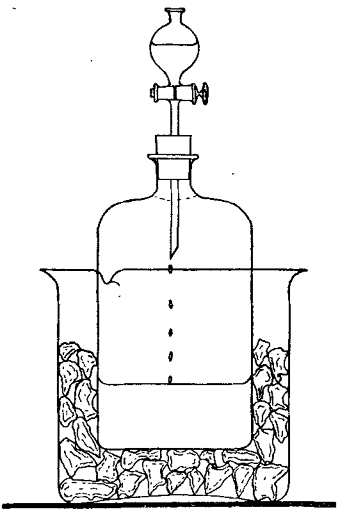


FIG. 50.

ing conc. sulphuric acid should be placed between the receiver and the pump to absorb aldehyde vapours, which would otherwise prevent a high vacuum being obtained.

$$CH_3.CHO + CH_3CHO \rightarrow CH_3.CHOH.CH_2.CHO.$$

*Yield.*—50% theoretical (50 gms.). Colourless, odourless liquid; D. $^0_4$ 1·12; B.P. $^{20}$ 75°. On distilling at atmospheric pressure forms acetaldehyde and much crotonaldehyde. (A., 306, 323; C., 1907, I., 1400; J. C. S., 117, 324.)

PREPARATION 43.—**Benzoin** (*α-Hydroxy-β-keto-αβ-diphenylethane*).

$$C_6H_5.CO.CH(OH).C_6H_5. \qquad C_{14}H_{12}O_2. \qquad 212.$$

21 gms. (2 mols.) of *pure* benzaldehyde and 2 gms. of 95% potassium cyanide dissolved in 80 c.cs. of 50% alcohol are refluxed for an hour on a water bath. The crystals of benzoin which separate on cooling are filtered off; 2 gms. of potassium cyanide are added to the filtrate and a second yield of benzoin obtained as before. The whole is recrystallised from hot alcohol.

$$2C_6H_5CHO \rightarrow C_6H_5CO.CH(OH).C_6H_5.$$

*Yield.*—90% theoretical (18 gms.). Colourless prisms; slightly soluble in water; soluble in alcohol and ether; M.P. 137°. (A., 198, 151; Am. Soc., 50, 2762; O. S., I., 33. See also J. C. S., 1928, 2483.)

**Reaction XXVI.** (*b*) **Condensing Action of Potassium Cyanide on a Mixture of an Aliphatic Aldehyde and a Ketone.** (A., 306, 324.)—This is a reaction similar to the previous, a ketone and an aldehyde being condensed to give a 1 : 3-ketol.

$$R.CO.CH_2R_1 + R_{11}CHO \rightarrow R.CO.CHR_1.CH(OH)R_{11}.$$

The ketone undergoing condensation must have at least one H attached to the α-C. If it has two, then, on heating, these ketols eliminate water to give olefinic ketones. It is to be noted that no condensation takes place at the oxy-carbon of the ketone. An excess of the ketone must always be used to minimise the condensation of two molecules of the aldehyde to an aldol compound. If the reaction is carried out at a high temperature, and with more powerful condensing agents, the unsaturated ketone is directly obtained (see Reaction XXIV.). (B., 25, 3165; C., 1905, II., 752.)

PREPARATION 44.—**Hydracetylacetone** (*δ-Hydroxy-β-keto-pentane*).

$$CH_3CH(OH)CH_2COCH_3. \qquad C_5H_{10}O_2. \qquad 102.$$

116 gms. (2 mols., excess) of *pure* acetone are cooled to − 12° (see p. 12) and treated with a 30% solution of 5 gms. of potassium cyanide. The mixture is then slowly stirred by mechanical means, and 44 gms. (1 mol.) of freshly prepared acetaldehyde dropped in, the temperature being kept below − 5°. The whole is allowed to stand for half an hour in the freezing mixture and 8 hours in an ice chest. 1½ vols. of alcohol-free ether are added, and the lower layer of potassium cyanide solution removed. Any remaining cyanide solution is extracted by washing twice with 60 c.cs. of saturated brine, and a third time with 30 c.cs. to ensure a complete extraction. The washing solution is extracted several times

with ether and the total ethereal solution dried for 2 hours over anhydrous sodium sulphate (calcium chloride absorbs hydracetylacetone). The ether is removed under reduced pressure and the residue fractionated three times under a pressure of 20 mms., first from 60°—110°, second 70°—90°, and third 77°—79°.

$$CH_3CHO + CH_3COCH_3 \rightarrow CH_3CH(OH)CH_2COCH_3.$$

*Yield.*—25% theoretical (25 gms.). Colourless, viscous liquid, miscible with water or alcohol ; can be salted out of aqueous solution by potassium carbonate ; B.P. $^{760}$ 176°—177° (slight decomposition) ; B.P. $^{20}$ 77°—78° ; D. $^{18}_{4}$ 0·9780. (A., 306, 324 ; B. 34, 2092 ; 37, 504 ; E.P., 435466.)

Note the use of 2 mols. of acetone to minimise aldol formation.

**Reaction XXVII. Condensation of Chloroform with Phenols and simultaneous Hydrolysis of the Product** (Reimer-Tiemann). (B., 15, 2585.) —This is a well-known method for the preparation of phenolic-aldehydes. The phenol is treated with chloroform and an alkaline hydroxide, when $-CHCl_2$ enters the *ortho*- and to a lesser extent the *para*-position to the hydroxyl group ; hydrolysis to an aldehyde then takes place.

$$C_6H_4\begin{matrix}\diagup ONa\\ \diagdown H\end{matrix} + Cl.CHCl_2 + NaOH \rightarrow C_6H_4\begin{matrix}\diagup ONa\\ \diagdown CHCl_2\end{matrix}$$

$$\downarrow$$

$$C_6H_4\begin{matrix}\diagup ONa\\ \diagdown CH(OH)_2\end{matrix}$$

$$\downarrow$$

$$C_6H_4\begin{matrix}\diagup OH\\ \diagdown CHO.\end{matrix}$$

Di-aldehydes can be obtained from some polyhydric phenols. Phenolic-ethers also react, as do hydroxy-aldehydes and hydroxy-acids.

Though it has such a wide application, the reaction suffers from many defects. The yields are poor, being of the order of 20% theoretical. This is due to the following causes :—

(*a*) A portion of the phenol does not react at all.

(*b*) Some forms an ester of ortho-formic acid—

$$3C_6H_5ONa + CHCl_3 = 3NaCl + CH(OC_6H_5)_3.$$

An excess of chloroform helps to prevent this.

(*c*) A portion of the aldehyde first formed is lost by condensation with some unattacked phenol to form a derivative of triphenyl methane—

$$C_6H_4\begin{matrix}\diagup CHO + 2HC_6H_4OH\\ \diagdown OH\end{matrix} = H_2O + CH(C_6H_4OH)_3.$$

To minimise this side reaction excess of phenol should be avoided.

(*d*) The alkali tends to react with the aldehyde formed, the more readily the higher the temperature.

The Reimer reaction is useless with compounds like phloroglucinol, pyrogallol, naphthols, poly-acid phenols of naphthalene, etc.

Accordingly, where possible (for the *p*-hydroxybenzaldehydes), the aluminium chloride method (Reaction XXVIII.) should be used. The yields are better, the reactions go more smoothly, little resin being formed, while pyrogallols and naphthols, etc., also react. Unfortunately, though the non-formation of other than *p*-hydroxyaldehydes is often an advantage, it limits the scope of the reaction and necessitates the use of the Reimer method in many cases. It should be noted that the nitro-phenols do not condense with chloroform (B., 9, 423, 824 ; 10, 1562 ; 15, 2685).

PREPARATION 45.—**Salicylaldehyde** (1 : 2-*Hydroxybenzaldehyde*) *and* 1 : 4-**Hydroxybenzaldehyde.**

$OH.C_6H_4.CHO.[1:2 \text{ and } 1:4]. \quad C_7H_6O_2. \quad 122.$

50 gms. (1 mol.) of phenol and 160 gms. (excess) of caustic soda in 160 c.cs. of water are heated to 50°—60° in a 1-litre flask on a water bath under a reflux. A thermometer dipping into the liquid is fitted to the flask. 75 gms. (excess) of chloroform are added, 10 c.cs. at a time, through the top of the condenser, the flask being well shaken after each addition. By alternate heating and cooling the temperature is kept at 65° throughout. The whole is then refluxed for half an hour, the excess of chloroform removed on a water bath, and the residue carefully acidified with dilute sulphuric acid and distilled in steam till no more oily drops pass over. The distillate is extracted with ether, and the extract shaken with twice its volume of a freshly prepared, nearly saturated solution of sodium hydrogen sulphite for a long time till no more crystals separate. (For preparation of bisulphite, see p. 510.) The precipitated bisulphite compound is filtered off, washed free from traces of phenol with alcohol and decomposed by heating on a water bath with dilute sulphuric acid. The aldehyde which separates is extracted with ether, the extract washed with water and dehydrated over anhydrous sodium sulphate. The ether is removed on a water bath and the aldehyde distilled. Some *p*-hydroxybenzaldehyde remains in the flask after the steam distillation. Tarry matter is removed by filtering hot through a moistened filter paper. The cold filtrate is extracted with ether, the extract dried over calcium chloride, the ether removed on a water bath, and the residue recrystallised from a small quantity of hot water containing sulphur dioxide.

$$C_6H_5.ONa + 3NaOH + CHCl_3 =$$
$$C_6H_4(ONa)CHO + 3NaCl + 2H_2O.$$

*Yield.*—*Salicylaldehyde*, 20% theoretical (13 gms.); 1 : 4-*Hydroxybenzaldehyde*, 4% theoretical (3 gms.) ; *total*, 24% theoretical (16 gms.).

*Salicylaldehyde.*—Colourless fragrant oil, soluble in water ; miscible in all proportions with alcohol and ether ; B.P. 196·5° ; solidifies to large crystals at 0° ; D. $^{15}_{4}$ 1·172.

p-*Hydroxybenzaldehyde*.—Colourless needles; soluble in hot water, alcohol and ether; M.P. 116°; sublimes. (B., 9, 824; 15, 2585.)

**Reaction XXVIII. Formation of an Aldime by the action of the compound of Hydrogen Chloride and Hydrogen Cyanide, HCN.HCl, on a Phenol or a Phenol Ether in the presence of Anhydrous Aluminium Chloride, and the Hydrolysis of the Aldime so formed** (Gattermann). (B., 31, 1765; 32, 271; A., 357, 363.)—As stated in Reaction XX. (*d*), the Gattermann-Koch reaction does not apply to phenols or phenol ethers. If it is desired to obtain aldehydes from them, hydrogen cyanide is used in place of carbon monoxide, and the mixture of anhydrous hydrogen cyanide and hydrogen chloride is allowed to act in presence of aluminium chloride alone, cuprous chloride being unnecessary. The crystalline compound, HCl.HCN, which hydrogen chloride forms with hydrogen cyanide, can also be used directly.

In order to avoid the preparation and handling of anhydrous hydrocyanic acid the passage of the gas direct from a generator (Am. Soc., 43, 348) and the use of zinc cyanide (Am. Soc., 45, 2373) have been tried with very satisfactory results.

$$\mathrm{HCN + HCl \rightarrow C}\begin{matrix}\diagup \mathrm{H} \\ = \mathrm{NH} \\ \diagdown \mathrm{Cl}\end{matrix}$$

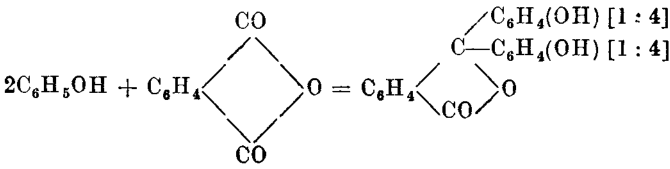
$$\mathrm{C_6H_4}\begin{matrix}\diagup \mathrm{OH} \\ \\ \diagdown \mathrm{H}\end{matrix} + \mathrm{ClCH:NH} \xrightarrow{\mathrm{AlCl_3}} \mathrm{C_6H_4}\begin{matrix}\diagup \mathrm{OH} \\ \\ \diagdown \mathrm{CH:NH.HCl.}\end{matrix}$$

The aldime hydrochloride so formed is very easily hydrolysed by acids to the aldehyde.

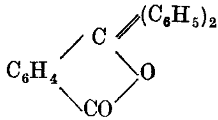
$$\mathrm{C_6H_4}\begin{matrix}\diagup \mathrm{OH} \\ \\ \diagdown \mathrm{CH:NH}\end{matrix} + \mathrm{H_2O} \rightarrow \mathrm{C_6H_4}\begin{matrix}\diagup \mathrm{OH} \\ \\ \diagdown \mathrm{CHO}\end{matrix} + \mathrm{NH_3}.$$

Combination always takes place in the *ortho*- and *para*-positions to the hydroxyl or alkoxyl group. (B., 55, 928; J. C. S., 1931, 84).

**Reaction XXIX.** (*a*) **Condensation of a Phenol with Phthalic Anhydride to form a Phthalein.** (A., 183, 1; 202, 68.)—The phthaleins result from the condensation of phthalic anhydride (1 mol.) with phenols (2 mols.) on heating with dehydrating agents—sulphuric acid, fused zinc chloride (to 120°) or anhydrous oxalic acid (to 115°). These compounds are particularly important; some are dyes of great technical value. The simplest representative of the class is phenolphthalein.

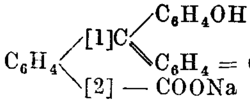


Thus the phthaleins are triphenylmethane derivatives, being all derived from phthalophenone (diphenyl phthalide).



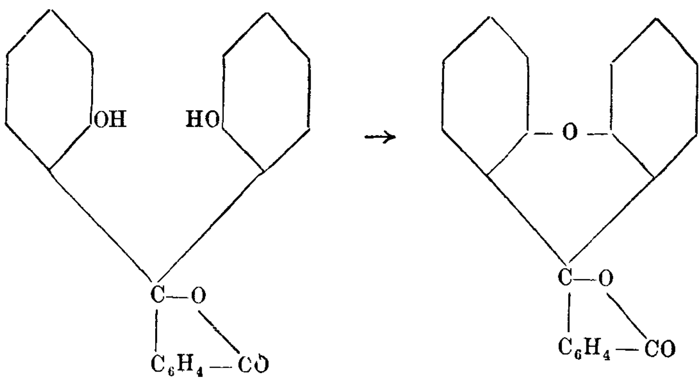

(See p. 86.)

The free phthaleins are usually colourless crystalline compounds dissolving with intense colorations in alkalis, but being reprecipitated by acids, even by $CO_2$. In very concentrated alkali they give colourless solutions. A quinone structure is assumed for the coloured salts, *e.g.*, for phenolphthalein in alkali solution.



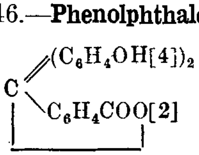

The phthaleins derived from di- or polyhydric phenols are all anhydrides formed by the elimination of water from two phenolic hydroxyls, attached to two different benzene rings. These "anhydride phthaleins" are known as pyronines, since they contain, like the pyrones, a six-membered oxygen-containing ring.

Even in the preparation of phenolphthalein a little of the simplest pyronine is obtained from an *ortho*-phthalein first formed.




From resorcinol the pyronine fluorescein is the main product (see p. 385).

Preparation 46.—**Phenolphthalein.**




$C_{20}H_{14}O_4$ 318.

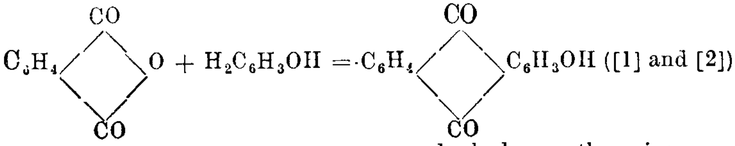
16 gms. conc. sulphuric acid are added to a mixture of 40 gms. (excess) of phenol and 20 gms. (1 mol.) of phthalic anhydride. The mixture is heated

for 9 hours at 115°—120° in an oil bath, and the red oil formed poured into a litre of water. The phenol is removed by continued boiling, water being added to replace that lost by evaporation. After cooling, the liquid is filtered and the residue washed with water. It is then dissolved in dilute caustic soda solution, and again filtered. The filtrate is acidified with acetic acid and a few drops of hydrochloric acid, and after standing for some time the precipitate is filtered off and dried. It is then refluxed on a water bath with an excess of absolute alcohol, a little animal charcoal being added if necessary. After filtration, the residue is washed with boiling absolute alcohol, and the combined filtrate and washings evaporated to two-thirds its bulk. It is diluted with 8 vols. of water and filtered through a wet filter to remove resinous matter. The filtrate is then concentrated on the water bath until the phenolphthalein crystallises.

$$2C_6H_5OH + C_6H_4(CO)_2O \longrightarrow C(C_6H_4COO)(C_6H_4OH)_2 + H_2O.$$

*Yield.*—25% theoretical (10 gms.). White crystalline powder; M.P. 250°—253°; slightly soluble in cold alcohol; soluble in alkalis to crimson solution. (B., 9, 1230; A., 183, 1; 202, 68.)

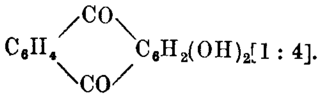
**Reaction XXIX.** (*b*) **Condensation of a Phenol with Phthalic Anhydride to a derivative of Anthraquinone.** (A., 212, 10.)—When equimolecular quantities of phthalic anhydride and a phenol react at 180° in the presence of conc. sulphuric acid, the product is not a phthalein, but the action takes a different course, and a derivative of anthraquinone is obtained.



α - and β-hydroxyanthraquinone.

Alizarin (1 : 2-dihydroxyanthraquinone) and an isomer, hystazarin (2 : 3-dihydroxyanthraquinone), are also formed in this way from catechol and phthalic anhydride.

PREPARATION 47.—**Quinizarin** (1 : 4-*Dihydroxyanthraquinone*).



$C_{14}H_8O_4$. **240.**

40 gms. (excess) phthalic anhydride and 10 gms. (1 mol.) of *pure* quinol are heated for 3 hours in a flask in an oil bath at 170°—180° with 200 gms. pure conc. sulphuric acid and 20 c.cs. of water. It is then heated for 1 hour at 190°—200°. The hot solution is gently poured into about a litre of cold water in a large basin. The whole is then heated to boiling and filtered hot with suction. The residue is again extracted with boiling water and filtered hot. It is then boiled up with 400 c.cs. glacial acetic acid and filtered hot, to remove carbonaceous matter. The filtrate is

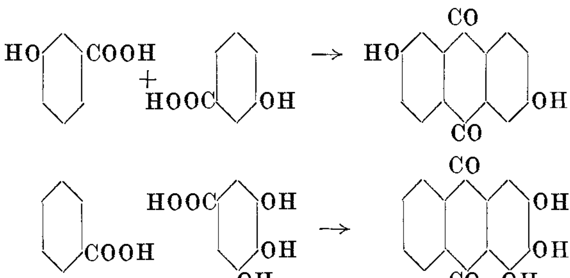
diluted with its own volume of hot water and filtered, the residue being again extracted with boiling glacial acetic acid and again precipitated with hot water. The crude quinizarin which separates on cooling is filtered, well washed with water and dried on a water bath. It is then quickly distilled from a hard glass retort with a large flame, a porcelain mortar being used as receiver. The distillate is then powdered and recrystallised from glacial acetic acid and washed with more dilute acetic acid and finally with water.

$$C_6H_4{<}\genfrac{}{}{0pt}{}{CO}{CO}{>}O + H_2C_6H_2(OH)_2 \rightarrow C_6H_4{<}\genfrac{}{}{0pt}{}{CO}{CO}{>}C_6H_2(OH)_2 + H_2O.$$

*Yield.*—20% theoretical (4 gms.). Dark red needles from toluene, orange-yellow leaves from glacial acetic acid; M.P. 195°; insoluble in water. (B., 8, 152; A., 212, 10; O. S., VI., 78.)

*Note.*—The quinizarin which solidifies in the neck of the retort may be recovered by distilling some glacial acetic acid from the retort, a distilling flask being used as receiver. Acetic acid vapour is inflammable, and care should be taken that it does not become ignited.

**Reaction XXIX.** (*c*) **Condensation of Meta-hydroxy- and di-meta-dihydroxy-benzoic Acids with themselves and with Benzoic Acid under the action of hot Sulphuric Acid.** (B., 18, 2147.)—The products of this action are hydroxyanthraquinones like the above.




These reactions are of interest as confirming the structure of anthraquinone and its hydroxy derivatives.

**Reaction XXX. Condensation of a Nitrile with a Phenol or a Phenol Ether and Hydrolysis of the resulting Ketimine Hydrochloride to a Ketone.** (J. C. S., 118, 309.)—This is a good method of synthesising phenolic ketones, and is an extension of the Gattermann method for phenolic aldehydes (Reaction XXVIII.). (B., 48, 1122; H. Acta., 4, 707.)

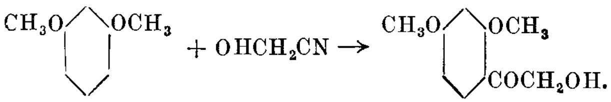
In 1915 Hoesch showed that the condensation of a nitrile with a phenolic compound led to the formation of a ketimine hydrochloride which could be easily hydrolysed to give a ketone.

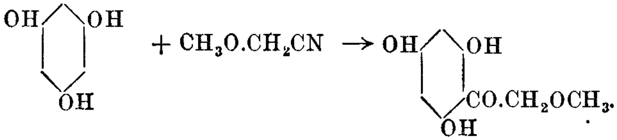
The phenol and the nitrile are dissolved in *dry* ether, and anhydrous hydrogen chloride led in. On standing, the hydrochloride of the ketimine

separates. Addition of fused zinc chloride is sometimes advantageous. The ketone is obtained on heating or boiling the hydrochloride with water. The ketimines themselves have also been isolated in some cases. They are unstable, and are hydrolysed on dissolving in water.

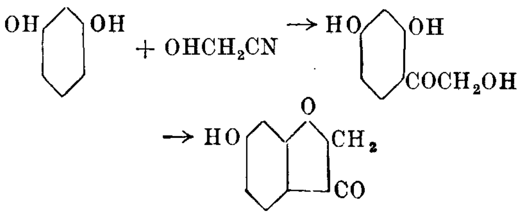
$$C_6H_5OH + C_6H_5.CH_2.CN \rightarrow [4]OHC_6H_4C(NH.HCl)CH_2C_6H_5 \rightarrow [4]OH.C_6H_4.CO.CH_2C_6H_5.$$

Condensation takes place in the *p*-position to the hydroxyl group. Di- and poly-hydric phenols and phenolic ethers can also be employed, as can hydroxy and methoxy nitriles (J. C. S., 118, 309).

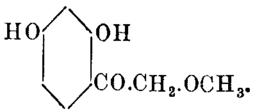




It is interesting to note that if a hydroxy nitrile be condensed with a di- or poly-hydric phenol, coumarone derivatives are obtained by elimination of water.



PREPARATION 48.—**ω-Methoxyresacetophenone** (*α-Methoxy-β-keto-β-*(2 : 4-*dihydroxyphenyl*) *ethane*).



$C_9H_{10}O_4$. 182.

6·5 gms. (1 mol.) of pure resorcinol are dissolved in 50 c.cs. of *anhydrous* ether and 5 gms. (1 mol.) of methoxyacetonitrile are added. A current of dry hydrogen chloride is passed through the solution for 2 hours, and the latter is allowed to stand in an ice chest for 5 days. The ether is then poured off from the yellow crystalline ketimine hydrochloride, which is washed twice with the same solvent and recrystallised from methyl alcohol. It forms a white crystalline mass (M.P. 205°—207°). It is dissolved in water and heated at 80° (not more, or tarry matter separates) for 30 minutes. The solution develops a deep red colour. On cooling, the ketone separates ; it is recrystallised from hot water.

$$C_6H_4(OH)_2[1:3] + CH_3OCH_2CN \rightarrow C_6H_3(OH)_2(CO.CH_2.OCH_3)[1:3:4].$$

*Yield.*—70% theoretical (8 gms.). Plates with nacreous lustre; soluble in alcohol, ether, benzene; insoluble in petrol ether; reduces Fehling's solution, forming copper mirror; M.P. 136°. (J. C. S., 118, 309.)

Resacetophenone and phloroacetophenone can be prepared from resorcinol and phloroglucinol, respectively, and acetonitrile in good yield (O. S., XV., 70).

1 gm. of fused zinc chloride can be added in the above reaction either initially or after the passage of the hydrogen chloride. It improves the yield and shortens the time of standing, but, unless care is taken, it tends to cause decomposition of the product during its isolation.

**Reaction XXXI. Action of Heat on Sodium Formate.** (B., 15, 4507.)—When sodium formate is rapidly heated above 440°, an unusual reaction takes place. It loses hydrogen and forms sodium oxalate.

$$\begin{matrix} HCOONa \\ + \\ HCOONa \end{matrix} = \begin{matrix} COONa \\ | \\ COONa \end{matrix} + H_2.$$

In the presence of sodium hydroxide, carbonates or oxalates, the reaction takes place at 360° and to a greater extent. (C., 1903, II., 777; 1905, II., 367.) Oxidation of formic acid with nitric acid similarly yields oxalic acid. (B., 17, 9.)

**Reaction XXXII. Action of Alkalis on certain α-di-ketones.** (A., 25, 25; 31, 324; B., 14, 326; 19, 1868; 41, 1644.)—When benzil is fused with potassium hydroxide, or digested with alcoholic potash, or heated for a long time with aqueous potash, a molecular re-arrangement not unlike the pinacoline transformation (p. 79) takes place, and benzilic acid is formed.

$$C_6H_5CO.CO.C_6H_5 \xrightarrow{H_2O} C_6H_5CO.C(OH)_2C_6H_5 \longrightarrow (C_6H_5)_2C(OH)CO.OH.$$

The acid can also be obtained directly from benzil by the action of air and caustic potash.

$$C_6H_5CH(OH)CO.C_6H_5 \xrightarrow{O\ +\ H_2O} (C_6H_5)_2C(OH)COOH.$$

Anisil and cuminil in a similar way yield anisilic and cuminilic acids.

PREPARATION 49.—**Benzilic Acid** (*Diphenylglycollic acid*).

$$(C_6H_5)_2C(OH).COOH. \qquad C_{14}H_{12}O_3. \qquad 228.$$

50 gms. (excess) of caustic potash are melted with a small quantity of water in a silver, nickel, or copper crucible. The liquid is allowed to cool to 150° (for combined thermometer and stirrer, and precautions to be taken in alkali fusions, see Fig. 53), and 10 gms. of dry, finely powdered benzil are added with constant stirring. The benzil melts and the whole soon sets to a solid mass of potassium benzilate. When all the oil has disappeared, the melt is cooled, dissolved in water, and benzilic acid precipitated by acidifying with hydrochloric acid. The precipitate is cooled with cold water and, to free it from traces of benzoic acid, is boiled in a dish with water until the smell of the latter has disappeared. On cooling,

benzilic acid separates, and is purified by recrystallisation from hot water.

$$C_6H_5CO.CO.C_6H_5 + KOH = (C_6H_5)_2C(OH)COOK.$$

*Yield.*—80% theoretical (16 gms.). See Preparation 50. (A., 25, 25; 31, 329; B., 14, 236; O. S., I., 29.)

PREPARATION 50.—**Benzilic Acid** (*Diphenylglycollic acid*).

$$(C_6H_5)_2C(OH).COOH. \qquad C_{14}H_{12}O_3. \qquad 228.$$

20 gms. (1 mol.) of benzil, 20 gms. (excess) of solid potassium hydroxide and 40 c.cs. of water are placed in a flask, and when the potash has dissolved, 50 c.cs. of alcohol are added. The mixture is then boiled for 10—12 minutes (not longer) on a boiling water bath; poured while still boiling into a beaker, and cooled and stirred to accelerate crystallisation. After half an hour's standing in ice, the crystals are filtered off at the pump through hardened filter paper, well pressed, and carefully washed with 40—50 c.cs. of ice-cold alcohol, so that the filtrate is finally almost colourless. The crystals are then dissolved in about 400 c.cs. of water, the solution filtered, brought to the boiling point, and 20 c.cs. of boiling dilute sulphuric acid are added. Part of the benzilic acid precipitates as an oil which, however, at once crystallises; the rest separates out in colourless needles on cooling the solution. It can be again recrystallised from hot water.

$$C_6H_5.CO.CO.C_6H_5 + KOH = (C_6H_5)_2C(OH).COOK.$$

*Yield.*—90% theoretical (20 gms.). Colourless needles; sparingly soluble in cold water; readily in hot water, and in alcohol; M.P. 150°. (B., 4, 1644.)

**Reaction XXXIII.** (*a*) **Condensation of an Aromatic Carboxylic Acid with Formaldehyde.** (Lederer-Manasse).—In the presence of mineral acids formaldehyde condenses to di-phenyl derivatives with aromatic acids in much the same way as with phenols (Reaction XIII.), except that in this case it is in the *meta* position the condensation takes place.

**Reaction XXXIII.** (*b*) **Condensation of Malonic Acids with Aldehydes or some Ketones under the influence of Primary or Secondary Amines.** (B., 35, 1143.)—This is an example of the activating effect of two 1 : 3-oxy groups on a methylene group between them. In the presence of primary or secondary amines—*e.g.*, ethylamine, di-ethylamine, piperidine—malonic acid condenses with aldehydes and some ketones to give unsaturated dicarboxylic acids. It is probable that the amine reacts first with the aldehyde, water being eliminated.

$$R.CHO + H_2NR_1 = R.CH : NR_1 + H_2O,$$

or

$$R.CHO + 2HNR_{11} = R.CH : (NR_{11})_2 + H_2O.$$

($R_{11}$ = a divalent or two monovalent radicals.)

The aldehyde derivative then acts on the acid to regenerate the amine,

$$RCH : NR_1 + CH_2(COOH)_2 = R.CH : C(COOH)_2 + NH_2R_1$$

or

$$RCH(NR_{11})_2 + CH_2(COOH)_2 = RCH : C(COOH)_2 + 2NHR_{11}.$$

In this way cinnamic aldehyde and malonic acid give cinnamylidene malonic acid.

$$C_6H_5.CH : CH.CHO + H_2C(COOH)_2 = C_6H_5CH : CH.CH : C(COOH)_2 + H_2O.$$

This latter, like all malonic acid derivatives, loses carbon dioxide on heating, and yields cinnamylidene acetic acid (see Preparation 427). For another and similar condensation brought about by amines, see Reaction XLV.

**Reaction XXXIII.** (*c*) **Condensation of Aldehydes with Malonic Acid in the presence of Alcoholic Ammonia.** (B., 31, 2604.)—When aldehydes are heated on a water bath with 1 mol. of malonic acid and 2 mols. of dilute alcoholic ammonia, condensation takes place as in the previous reaction, but elimination of carbon dioxide occurs simultaneously so that an unsaturated derivative of acetic acid is formed.

$$C_6H_5.CHO \xrightarrow{NH_3} C_6H_5.CH : NH \xrightarrow{CH_2(COOH)_2}$$
$$C_6H_5CH : C(COONH_4)_2 \rightarrow C_6H_5CH : CHCOONH_4$$
$$\rightarrow C_6H_5CH : CHCOOH.$$

In this way, also, crotonaldehyde yields sorbic acid (B., 33, 2140).

$$CH_3.CH : CH.CHO \rightarrow CH_3.CH : CH.CH : C(COOH)_2$$
$$\rightarrow CH_3CH : CH.CH : CHCOOH.$$

PREPARATION 51.—**Cinnamic Acid** (*β-Phenylacrylic acid*).

$$C_6H_5CH : CH.COOH. \qquad C_9H_8O_2. \qquad 148.$$

20 gms. (1 mol.) of benzaldehyde and 80 gms. (2 mols. of $NH_3$) of an 8% solution of ammonia in alcohol, are added to 20 gms. (1 mol.) of malonic acid. The mixture is heated on a water bath until a clear solution is obtained. The alcohol is then removed by evaporation and heating continued until the evolution of carbon dioxide ceases. The residue is dissolved in water, and cinnamic acid precipitated by adding hydrochloric acid. It is then purified as in Preparation 52.

$$C_6H_5CHO + H_2C.(COOH)_2 \rightarrow C_6H_5CH : CH.COOH + CO_2 + H_2O.$$

*Yield.*—80% theoretical (22 gms.) (see p. 115). (A., 188, 194 ; B., 31, 2604.)

**Reaction XXXIII.** (*d*) **Condensation of Aldehydes with the Sodium Salts of certain Acids in the presence of Acid Anhydrides** (Perkin). (A., 100, 126 ; 227, 48 ; B., 10, 68 ; 14, 1826 ; J. C. S., 21, 53 ; J., 1877, 789.) —This is a reaction of very wide application, and one much used in the preparation of unsaturated aromatic carboxylic acids. It consists in heating together—usually to 180°—an aldehyde, the sodium salt of a fatty acid with at least one α-hydrogen atom, and an acid anhydride. The following reactions then occur :—

(i.) Condensation takes place between the α-carbon of the acid salt and the aldehydic carbon (*cf.* the aldol condensation, p. 101).

$$R.CHO + R_1.CH_2.COONa \rightarrow R.CH(OH).CHR_1.COONa.$$

The hydroxy acid so formed is stable if: (*a*) the α-carbon of the original acid has only one hydrogen atom attached, *e.g.*,

$$C_6H_5.CHO + (CH_3)_2.CHCOONa \rightarrow C_6H_5CH(OH)C.(CH_3)_2COONa.$$

or (*b*) it is a α-hydroxy acid, and so immediately forms a stable lactone. This occurs when sodium succinate is employed.

$$C_6H_5.CHO + \begin{array}{l} CH_2.COONa \\ | \\ CH_2COONa \end{array} \rightarrow C_6H_5.CH.(OH).CH.(COONa).CH_2.COONa.$$

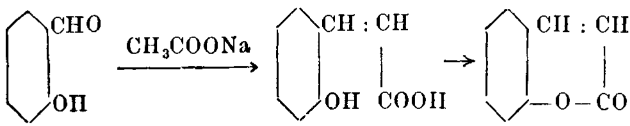
$$\rightarrow C_6H_5.CH(OH).CH(COOH).CH_2.COOH \rightarrow \begin{array}{l} C_6H_5.CH.CH(COOH) \\ \quad\;\;\; | \quad\;\; | \\ \quad\;\;\; | \quad\; CH_2 \\ \quad\;\;\; | \quad\;\; | \\ \quad\;\;\; O{-}{-}CO \end{array}$$

Phenylparaconic Acid.

(ii.) Except in the above cases, elimination of water occurs and an α β unsaturated acid is formed.

$$R.CH(OH).CHR_1.COONa \rightarrow R.CH : CR_1.COONa.$$

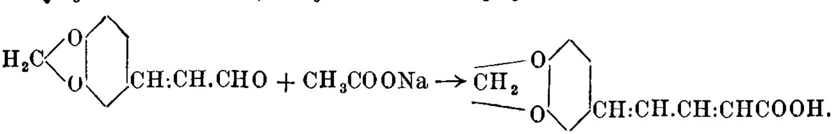
(iii.) If an *ortho*-phenolic aldehyde is used, a further loss of water takes place with the formation of a lactone.




Although the anhydride used need not be that of the acid of which the Na salt is used, it is best to have it so; otherwise there is a liability to double decomposition between the sodium salt and the anhydride, giving both sodium salts and both anhydrides, thus leading to a mixture of condensation products. A low temperature helps to prevent such decomposition.

Both substituted aldehydes and acids may be used so that the reaction is capable of numerous modifications. The following equations will illustrate this—

$$C_6H_5CHO + CH_2ClCOONa \rightarrow C_6H_5.CH : CCl.COOH.$$
$$C_6H_5.CH : CH.CHO + CH_3COONa \rightarrow C_6H_5CH : CH.CH : CHCOOH.$$




Piperic Acid.

Aliphatic aldehydes may also be used in this reaction, but react with difficulty.

PREPARATION 52.—**Cinnamic Acid** (*β-Phenylacrylic acid*).

$C_6H_5.CH : CH.COOH. \quad C_9H_8O_2. \quad 148.$

20 gms. (excess) of benzaldehyde, 30 gms. (excess) of acetic anhydride, both freshly distilled, and 10 gms. (1 mol.) of freshly prepared powdered anhydrous sodium acetate (see p. 509) are refluxed together for 8 hours in a 250-c.c. round-bottomed flask (fitted with a wide vertical air-condenser about 60 cms. long) in an oil bath, kept at 180°. A calcium chloride tube is fitted to the top of the condenser. The experiment need not be completed in one day; when finished, the hot reaction mixture is poured into a 1-litre round-bottomed flask, sodium carbonate is added till alkaline, and then water until the bulk is 5 times the original. The whole is then steam distilled until no more benzaldehyde comes over. The residue is filtered hot through a wet, folded filter paper to remove oily and resinous by-products, cooled, and acidified with dilute hydrochloric acid. The precipitated cinnamic acid is purified by reprecipitation from alkaline solution or by recrystallisation from hot water.

$$C_6H_5.CH{:}O + CH_3.COONa \rightarrow C_6H_5.CH(OH).CH_2.COONa \rightarrow$$
$$C_6H_5.CH : CH.COONa \rightarrow C_6H_5.CH : CH.COOH.$$

*Yield.*—85% theoretical (15 gms.). Crystallises from hot water in fine needles; from alcohol in thick prisms; readily soluble in hot water; M.P. 133°; B.P. $^{760}$ 300°. (A., 227, 48; J. C. S., 21, 53; B., 16, 1436.)

Malonic acid condenses especially readily. Even at ordinary temperatures, in presence of acetic anhydride, it yields benzalmalonic acid with benzaldehyde. Better results are obtained, however, by using a less powerful condensing agent—glacial acetic acid—at 100°. This synthesis is interesting as providing a method for the preparation of certain monobasic acids, since all malonic acids readily lose carbon dioxide on heating (see Preparation 427).

PREPARATION 53.—**Benzylidenemalonic acid** (*α-Phenylethen-ββ-di-acid*).

$C_6H_5CH : C(COOH)_2. \quad C_{10}H_8O_4. \quad 192.$

4 gms. of glacial acetic acid, 7 gms. (1 mol.) of benzaldehyde and 7 gms. (1 mol.) of malonic acid are heated together for 10 hours at 100° under a reflux. On cooling, benzalmalonic acid separates out, is filtered off and washed with chloroform.

$$C_6H_5CHO + H_2C(COOH)_2 \rightarrow C_6H_5CH : C(COOH)_2 + H_2O.$$

*Yield.*—40% theoretical (5—6 gms.). Colourless crystals; M.P. 196° with decomposition; insoluble in chloroform; is converted to cinnamic acid at 200°—210°. (A., 218, 129.)

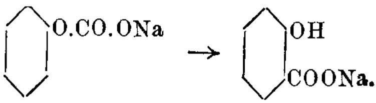
**Reaction XXXIII.** (*e*) **Condensation of the Dichlorides of Aromatic Aldehydes with the Sodium Salts of certain Acids.** (B., 15, 969.)—This is a modification of the previous reaction used commercially to prepare cinnamic acid, by heating sodium acetate with benzal chloride. The latter is much cheaper than benzaldehyde.

$$C_6H_5.CHCl_2 + CH_3.COONa = C_6H_5.CH : CH.COONa + NaCl + HCl.$$

**Reaction XXXIV.** (*a*) **Condensation of Carbon Dioxide with a Phenol** (Kolbe and Schmitt). (J. pr., [2] 10, 89; 27, 39; 21, 397.)—When carbon dioxide is passed over *dry* sodium phenolate at 110°, sodium phenylcarbonate is obtained.

$$C_6H_5ONa + CO_2 = C_6H_5O.CO.ONa.$$

If the temperature be then slowly raised to 190°, intramolecular re-arrangement takes place, and monosodium salicylate is formed. This, at ordinary pressures, reacts with unchanged sodium phenolate to produce di-sodium salicylate and phenol.




$$C_6H_4(OH)(COONa) + C_6H_5ONa = C_6H_4(ONa)(COONa) + C_6H_5OH$$

This is "Kolbe's synthesis" of phenolic acids. It is capable of very wide application. In all cases the carboxyl group primarily seeks the *ortho*-position; if that is occupied, some condensation in the *para*-position occurs. The following are some examples.

(i.) Phenolic ethers also react, *e.g.*, sodium guaiacolate gives 3-methoxy-2-hydroxybenzoic acid.

(ii.) The polyhydric phenols react especially easily. Boiling with an aqueous solution of ammonium carbonate or under pressure with aqueous potassium carbonate is sufficient. (M., 1, 236, 468; 2, 448, 458.)

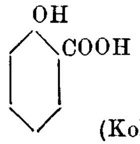
$$C_6H_4(OH)_2 + OH.COOK = C_6H_3(OH)_2COOK + H_2O.$$

(iii.) $\alpha$- and $\beta$-naphthols yield hydroxynaphthoic acids.

It is an interesting fact that if potassium phenolate is used in the Kolbe synthesis *para*-hydroxy benzoic acid is obtained, especially at high temperatures. Potassium phenyl carbonate is first formed, and heated up to 150° yields salicylic acid, but if the temperature be further raised, the *para*-acid is produced in increasing quantities until at 220° potassium *para*-hydroxy-benzoic acid is the sole product.

It will have been noted that in the formation of salicylic acid, only one half of the phenol is converted; the rest is obtained unchanged. Schmitt (*Dingler's Polytechnisches Journal*, 255, 259) succeeded in modifying the synthesis to obviate this defect, and his is the method always used industrially, although the other is more convenient in the laboratory. In Schmitt's synthesis sodium phenyl carbonate is prepared by heating up to 120°—140° dry sodium phenolate with carbon dioxide in autoclaves under pressure. Complete transformation of the intermediate sodium phenyl carbonate to mono-sodium salicylate then occurs on further heating. The carbon dioxide may be led in from a cylinder under pressure, or liquid or solid carbon dioxide may be mixed directly with the sodium phenolate in the autoclave. If preferred, the sodium phenyl carbonate can be prepared at ordinary pressures at 110° and then heated under pressure at 140°.

PREPARATION 54.—**Salicylic Acid** (1-*Hydroxy*-2-*carboxybenzene*).



$C_7H_6O_3$. 138.

(Kolbe's Method.)

10 gms. (2 mols.) of pure sodium hydroxide are dissolved in 15 c.cs. of water in a metal basin, and, with stirring, 23 gms. (2 mols.) of crystallised phenol are gradually added. The solution is then heated over a small free flame, with continual stirring, until a crystalline film forms on the surface of the liquid. Evaporation is continued by heating with a luminous flame kept in constant motion. During the process the basin should be securely clamped. A caked mass is obtained which is crushed at intervals with a pestle. When the mass no longer cakes together, it is transferred to a dry warm mortar and pulverised as it cools. The powder, while still warm, is quickly returned to the basin, and heated as before with thorough stirring, until it is dry enough to form dust. It is then immediately placed in a 200-c.c. tubulated retort, where it is heated in a bath to 140° in a fairly rapid current of dry hydrogen (*caution*) obtained from a Kipp generator.

When in about 1 hour no more moisture condenses in the neck of the retort, and the body of the retort appears dry, the mass is allowed to cool in the current of hydrogen and then, while still warm, broken up, removed, quickly powdered in a mortar, and replaced. The object of the above operations is to obtain perfectly dry, uncharred, well-powdered sodium phenate, for it is on these factors that the success of the whole preparation depends. A moderate stream of carbon dioxide, dried through two wash bottles of conc. sulphuric acid, is passed over the surface of the sodium phenate by means of a bent tube fixed through the tubulus of the retort, and terminating 1 cm. above the substance. The retort is immersed as far as possible in the oil bath, and the temperature gradually raised to 110° and kept there for 1 hour. The temperature is then raised to 190° in 4 hours, and on to 200°, where it is kept for 2 hours. During the whole operation, the mass is stirred frequently with a glass rod momentarily inserted through the tubulus, and the retort also shaken from time to time, to ensure that fresh surfaces shall be exposed to the action of the gas. During the heating phenol distils and collects in the neck of the retort while the contents darken in colour. On cooling, the phenol is melted by application of a flame to the outside of the neck and allowed to flow away; then the crude reaction product is shaken out through the tubulus into a large beaker, and the retort washed out several times with warm water. The whole is boiled, filtered if necessary, and treated with much conc. hydrochloric acid (100 c.cs.), cooled for some hours in ice-water, and precipitation of the crude salicylic acid facilitated by rubbing the sides of the vessel with a glass rod. The precipitate is filtered off at the pump, washed with a little cold water, and dried on a porous plate. The filtrate is eva-

porated to low bulk, and a little more acid obtained. It may be purified by recrystallising from boiling water with the addition of animal charcoal, but it is better to distil the crude acid with superheated steam (see p. 25). The crystals are *thoroughly* dried, first on a porous plate, and then by heating on a water bath. They are placed in a short-necked flask and heated in an oil bath of 170°. Then connection is made to the steam generator and a moderate current of steam at 175° pressed in. It is important that the steam generator be not connected to the flask till the oil bath and steam have the same temperature. A wide condenser is used (width of inner tube 3 cms.; of outer jacket 6 cms.; length of latter 80 cms.), otherwise the condensing acid soon blocks it. The connecting tube between the flask and condenser must be 2·5 cms. wide, and as short as possible. The side-piece should be near the bulb. When no more acid distils, the crystals in the condenser are added to the distillate, which is boiled and filtered. The acid separates on cooling.

$$C_6H_5O.CO.ONa + C_6H_5ONa = C_6H_4\begin{cases} ONa \\ CO.ONa \end{cases} + C_6H_5OH.$$

*Yield.*—60% theoretical, allowing for phenol recovered (10 gms.). Colourless needles; soluble in alcohol and hot water; volatile in steam; much used in industry as an antiseptic and a dye intermediate; yields phenol on heating; M.P. 158·5°. (B., 8, 537; Dingl. Poly. J. (1885), 255, 259; D.R.P., 38, 742; E.P., 353464.) (J. pr., [2], 10, 95; 27, 39; 31, 397.)

For purification, see E.P., 353921.

**Reaction XXXIV.** (*b*) **Action of Carbon Dioxide on an Organo-magnesium Halide** (Grignard). (B., 35, 2519; 39, 634; 40, 1584.)—When an alkyl or aryl magnesium bromide or iodide dissolved in *dry* ether is treated with *dry* carbon dioxide, the mono-carboxylic acid of the next higher series is formed. Like all "Grignards" (see pp. 66, 72, 95) this reaction is of very general application. It works better with iodides than with bromides, and with aryl rather than alkyl compounds. The general remarks on the other Grignard reactions apply here. Moisture must be absent, iodine can be used as a catalyst and so on. Also the reaction takes place in two stages, the usual intermediate compound being obtained.

$$R.Mg.I + CO_2 = R.COOMgI.$$
$$R.COOMgI + H_2O = R.COOH + OH.MgI.$$

Either acid or alkali can be used to hydrolyse the intermediate compound. The yields in most cases are good, but the reaction can sometimes take another course. (B., 40, 1584.)

Before the following three preparations are attempted, the methods for each should be studied and compared.

PREPARATION 55.—**Propionic Acid** (*Propan acid*).

$$CH_3.CH_2.COOH. \qquad C_3H_6O_2. \qquad 74.$$

All vessels used in this experiment must be absolutely *dry*. 12 gms. (1 mol.) of *dry* bright magnesium turnings (see Preparation 19) are dis-

solved in a solution of 28 gms. (1 mol.) of *dry* ethyl iodide in 20 c.cs. of *dry* ether (see p. 216) contained in a flask fitted with a reflux condenser. The action may, if necessary, be started by adding a crystal (0·05 gm.) of iodine; should it become too vigorous, it is moderated by cooling in water. When all the magnesium has dissolved, a not too rapid stream of carbon dioxide, washed once with sodium carbonate solution, twice with conc. sulphuric acid, and passed then over phosphorus pentoxide, is led in until it ceases to be absorbed, the flask being cooled if required. The ether is removed on a water bath and the residue distilled with dilute sulphuric acid (water is added as required) until the distillate is no longer acid. The propionic acid may be isolated by forming the lead salt, proceeding as in Preparation 473, or the aqueous solution may be treated with excess of sodium carbonate and evaporated to dryness. The powdered residue is then distilled with conc. sulphuric acid until the temperature reaches 155°. The distillate is again distilled, the fraction 137°—142° being retained.

$$C_2H_5I + Mg = C_2H_5.Mg.I.$$
$$C_2H_5.Mg.I + CO_2 = C_2H_5.COOMgI.$$
$$C_2H_5.CO.OMgI + H_2O = C_2H_5.COOH + (OH)MgI.$$

*Yield.*—50% theoretical (7 gms.). Colourless liquid; rancid acid odour; M.P. 24°; B.P. 141°; D. $^0_4$ 1·013.

The yield increases with aryl-compounds, as may be seen from the two following preparations.

PREPARATION 56.—**Benzoic Acid** (*Benzene*mono*carboxylic acid*).

$C_6H_5.COOH$. $C_7H_6O_2$. 122.

2·6 gms. (1 mol.) of clean magnesium powder (or thin shavings or ribbon about 2 mms. in width, each piece about 1 cm. long, cleaned with fine emery paper and then with filter paper) are dried in an air oven at 110° for 20 minutes and placed in a dry flask fitted with a reflux. A mixture of 40 c.cs. of *dry* ether (see p. 216) and 20·4 gms. (1 mol.) of *dry* iodobenzene of constant boiling point, and a crystal of iodine are then added. The flask is dipped in hot water or heated on a water bath so that the ether boils gently.

In about half an hour a white flocculent precipitate begins to form, and when the heat of the reaction makes the ether boil vigorously, the water bath is removed. The flask is now wrapped in a dry cloth to conserve the heat of the reaction, and in the course of 2 hours the magnesium is practically all dissolved. (If this does not occur, traces of moisture are probably present, and the experiment must be repeated, the ether being distilled off and again dried over sodium.) When the boiling of the ether slackens, the flask is reheated for half an hour as before on a water bath.

The flask is then cooled in ice-water, the condenser removed, and a slow current of carbon dioxide, washed and dried as in the previous experiment, led into the ethereal solution, which may still contain traces of undissolved magnesium. The cooling must be continued throughout the

operation. The reaction mixture forms two layers, an upper layer of ether, and a heavy resinous lower layer of the reaction product. If the gas current is too rapid, only a slight layer of resinous mass will be obtained, but the preparation will still succeed if the cooling be thorough. Powdered ice is now added, and then, slowly, 30 c.cs. (excess) hydrochloric acid (15%). The precipitated benzoic acid is extracted with ordinary ether, the latter removed on a water bath, and the residue gently warmed with dilute caustic alkali. The undissolved portion (see B., 49, 1584) is filtered off, and the benzoic acid reprecipitated with hydrochloric acid. More acid is obtained by extracting the mother liquor with ether. The whole is recrystallised from hot water.

$$C_6H_5I \rightarrow C_6H_5.Mg.I \rightarrow C_6H_5.CO.O.MgI \rightarrow C_6H_5.COOH.$$

*Yield.*—90% theoretical (11 gms.). Colourless needles; soluble in hot water, and in alcohol and ether; volatile in steam; M.P. 122°; B.P. 250°. (B., 38, 2759.)

$CO_2$ can also be combined directly with benzene in presence of aluminium chloride to yield benzoic acid. (A. Ch., [6], 14, 441.)

PREPARATION 57.—**Triphenylacetic Acid** (*Triphenylethan acid*).

$$(C_6H_5)_3C.COOH. \qquad C_{20}H_{16}O_2. \qquad 288.$$

10 gms. (1 mol.) of triphenyl chloromethane (see p. 432) and 0·05—0·1 gm. of iodine are dissolved by gentle heating in 50 c.cs. of ether, dried as on p. 216. 2 gms. ($2\frac{1}{2}$ mols.) of *clean, dry* magnesium powder (see Preparation 18) are added, and the whole boiled under a reflux while a not too rapid current of *dry* carbon dioxide (see Preparation 55) is led into the liquid. After 3 hours, a lemon-yellow precipitate of the complex magnesium compound has formed. While the carbon dioxide is passing in, the whole is frequently shaken up, and dry ether is added to replace that removed by the carbon dioxide. To decompose the complex magnesium compound, 60 c.cs. of water are added to the flask, and the whole well shaken, poured into a basin, gradually treated with 40 c.cs. of conc. hydrochloric acid to dissolve the excess of magnesium, and boiled for 3 minutes, during which it is well shaken. The crude acid is filtered off on cooling, washed and boiled in a porcelain basin with 200 c.cs. (excess) of a 10% caustic soda solution and 100 c.cs. of water, when the greater portion of the acid goes into solution. The mixture is diluted with 300 c.cs. of water, cooled, filtered, and 100 c.cs. of conc. hydrochloric acid added. The liquid is heated to make the somewhat gelatinous precipitate granular, cooled, the acid filtered off, washed and dried. It is recrystallised from glacial acetic acid.

$$(C_6H_5)_3CCl \rightarrow (C_6H_5)_3CMgCl \rightarrow (C_6H_5)_3CCOOMgCl \rightarrow (C_6H_5)_3C.COOH.$$

*Yield.*—83% theoretical (8·5 gms.). Long glittering prisms; sparingly soluble in water, ether or benzene; M.P. 264°—265°. (B., 39, 634.)

For a résumé of some other applications of Grignard reagents, see J. S. C. I., 41, 7.

**Reaction XXXIV.** (*c*) **Action of Carbon Dioxide on Sodium Acetylides in Dry Ether.** (B., 12, 853 ; J. pr., [2], 27, 417 ; B., 33, 3586.)—This is an example of the great activating influence of a triple bond. When carbon dioxide is passed into a solution of the sodium derivative of an acetylenic hydrocarbon in *dry* ether, direct addition takes place to give the sodium salt of the next highest acetylenic carboxylic acid. For example, sodium allylene yields sodium tetrolate—

$$CH_3C \vdots CNa \rightarrow CH_3.C \vdots C.COONa,$$

and sodium phenyl-acetylene gives sodium phenyl-propiolate—

$$C_6H_5C \vdots CNa \rightarrow C_6H_5.C \vdots C.COONa.$$

This reaction should be compared with the preceding one. It should be noted that the presence of a triple bond attached to a carbon makes a hydrogen attached to that carbon replaceable by a metal (*cf.* Reaction XXIII. (*a*) ).

**Reaction XXXV.** (*a*) **Condensation of Phthalic Anhydride with Aromatic Hydrocarbons in the presence of Anhydrous Aluminium Chloride** (Friedel-Crafts). (A., 291, 9 ; C. r., 119, 139.)—When the dichloride of phthalic anhydride reacts with the hydrocarbon, benzene, in presence of anhydrous aluminium chloride, phthalophenone (diphenylphthalide) is formed (see p. 107). With phthalic anhydride itself the reaction can be made to take the same or a different course. Using an excess of hydrocarbon, condensation and hydrolysis occur, and *o*-benzoyl-benzoic acid or its homologues are obtained according to the reacting hydrocarbon. Not only can the latter be varied, but derivatives of phthalic anhydride may be used, so that a great number of compounds can be synthesised in this way.

$$C_6H_4\left\langle\begin{array}{l}CO\\CO\end{array}\right\rangle O + C_6H_6 \xrightarrow{AlCl_3} C_6H_4\left\langle\begin{array}{l}COC_6H_5\\COOH.\end{array}\right.$$

The *ortho*-benzoyl-benzoic acids readily yield anthraquinone and its derivatives (see p. 82). It may be noted that *o*-benzoyl-benzoic acid itself, with benzene and aluminium chloride, yields phthalophenone ; the same compound is made directly from phthalic anhydride by increasing the amount of the latter or by adding acetic anhydride. The same holds for *p*-toluoylbenzoic acid and ditoluoylphthalide. (Am. Soc., 43, 1965 ; J. C. S., 122, 539.) (For the use of carbomethoxylbenzoyl chlorides and of homophthalic anhydrides in these reactions, see Am. Soc., 43, 1950.)

Succinic and glutaric anhydrides condense with benzene in similar manner (O. S., XIII., 12.)

PREPARATION 58.—*o*-**Benzoylbenzoic Acid** (*Diphenyl ketone-2-dicarboxylic acid*).

$$C_6H_4\left\langle\begin{array}{ll}COC_6H_5 & [1]\\COOH & [2]\end{array}\right. \qquad C_{14}H_{10}O_3. \qquad 226.$$

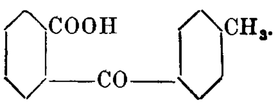
175 gms. (excess) of dry benzene are added to 50 gms. (1 mol.) of finely powdered phthalic anhydride. To this are added 90 gms. fresh aluminium

chloride and the mixture is gently heated on a water bath in a flask fitted with a good mechanical agitator and a reflux condenser (see Fig. 38). The reaction is moderated by cooling. When the mass becomes viscous, the temperature is raised to 70° and kept there till the evolution of hydrochloric acid ceases. The mechanical agitator is removed and an ordinary condenser attached. Four volumes of cold water are gradually added through a tap funnel, and the heat evolved causes most of the unchanged benzene to distil over. Steam is then passed through the mixture to remove the remainder of the benzene, and the residue is boiled for 4 hours, caustic soda solution being added to make slightly alkaline. The precipitated alumina, formed by the decomposition of the aluminium compound, is filtered off and washed with boiling water. The filtrate which contains the sodium salt of *o*-benzoylbenzoic acid is then acidified with dilute hydrochloric acid, and the free acid filtered off. It is then recrystallised from water.

$$C_6H_4\begin{matrix}\diagup CO \diagdown \\ \diagdown CO \diagup\end{matrix}O + C_6H_6 \xrightarrow{AlCl_3} C_6H_4\begin{matrix}\diagup CO-C_6H_5 \\ \diagdown COOH.\end{matrix}$$

*Yield.*—95% theoretical (72 gms.). Colourless crystals; M.P. 127° when anhydrous; contains $1H_2O$ when crystallised from water, M.P. 94°. (A., 291, 9; B., 14, 1865; 41, 3631.)

PREPARATION 59.—**2-*p*-Toluoylbenzoic Acid** (*4-Methyldiphenyl ketone-2′-carboxylic acid*).



$C_{15}H_{12}O_3$. 240.

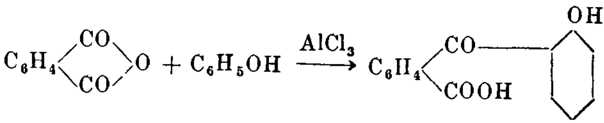
50 gms. (1 mol.) of finely powdered phthalic anhydride and 200 gms. (excess) of dry redistilled toluene are mixed together, and 100 gms. (excess) of finely powdered, freshly prepared, anhydrous aluminium chloride (see p. 506) are added all at once. Hydrogen chloride is evolved, and the mixture becomes warm. After 10 hours, water is added, and excess of toluene removed by steam distillation. The aqueous solution is poured off (from it a little phthalic acid may be removed by acidification), and the remaining cake is treated with sodium carbonate till alkaline. Steam is passed in for 5 hours to decompose the aluminium compound, the whole filtered, and the filtrate acidified whereby 2-*p*-toluoylbenzoic acid is precipitated.

$$C_6H_4\begin{matrix}\diagup CO \diagdown \\ \diagdown CO \diagup\end{matrix}O + C_6H_5.CH_3 \xrightarrow{AlCl_3} C_6H_4\begin{matrix}\diagup COC_6H_4CH_3 \\ \diagdown COOH(AlCl_3)\end{matrix}$$

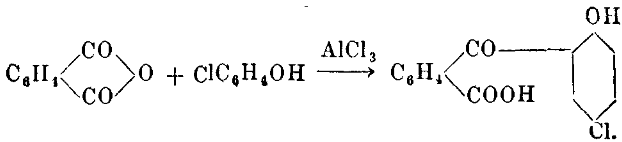
$$\rightarrow C_6H_4\begin{matrix}\diagup COC_6H_4.CH_3 \\ \diagdown COOH.\end{matrix}$$

*Yield.*—97% theoretical (78 gms.). Colourless crystals; insoluble in cold water; M.P. 146°. (B., 41, 3632; J. pr., [2], 33, 318; A., 311, 178.

**Reaction XXXV.** (*b*) **Condensation of Phthalic Anhydride with Phenols in the presence of Anhydrous Aluminium Chloride, *s*-tetrachloroethane being used as a Solvent.** (B., 52, 2098; 53, 826.)—This is an extension of the previous reaction to phenols; employment of tetrachloroethane as solvent has enabled satisfactory yields to be obtained. Condensation takes place in the *ortho*-position to the hydroxyl group. Thus phenol and phthalic anhydride yield 2-(*o*-hydroxybenzoyl)-benzoic acid.



and *p*-chloro-phenol and phthalic anhydride give 2-(2-hydroxy-5-chloro-benzoyl)-benzoic acid.



This reaction is specially interesting since many of the above compounds readily yield the corresponding anthraquinone derivatives (see p. 82), *e.g.*, 4-chloro-1-hydroxy-anthraquinone has been obtained from *p*-chloro-phenol; substituted anthraquinones of this type are becoming increasingly important.

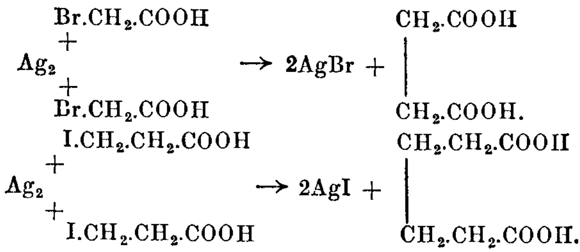
**Reaction XXXVI. Condensation of Carbon Tetrachloride with Phenols and simultaneous Hydrolysis** (Tiemann-Reimer). (B., 10, 2185.)—This reaction is closely analogous to that of the formation of hydroxy-aldehydes by means of chloroform and caustic alkali (see p. 104). A mixture of a phenol, carbon tetrachloride and caustic soda or caustic potash solution is boiled. Condensation occurs, chiefly in the *para*-position, but small amounts of the *ortho*-acids are also formed. The product, after the excess of carbon tetrachloride has been removed, is saturated with carbon dioxide and the unchanged phenol extracted with ether. The hydroxy acids are then precipitated by acidification with hydrochloric acid.

$$C_6H_5OH + CCl_4 + 5KOH = C_6H_4\begin{cases} OH \\ COOK \end{cases} + 4KCl + 3H_2O.$$

A variation of this method consists in heating carbon tetrachloride with potassium phenolate under pressure with sufficient alcohol to give a clear solution. The product in this case is mostly the *ortho*-acid (*cf.* Reaction XXXIV. (*a*)).

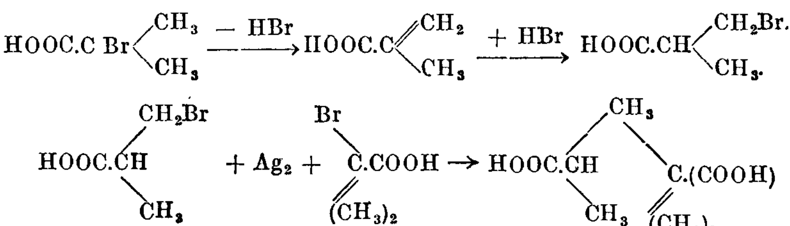
**Reaction XXXVII. Action of finely divided Metals on Halogen Acids.** (B., 2, 720; 28, R., 466.)—The use of metals—sodium, copper, silver—to eliminate halogen from halogen compounds, and bring about the condensation of the carbons to which the halogen atoms are attached has, as

is well known, a very wide application. It is employed as a standard method with the halogen acids which react readily, to obtain many of the higher dibasic acids. Thus bromacetic acid on heating with finely divided metallic silver yields succinic acid; $\beta$-iodo-propionic acid in a similar manner gives adipic acid with silver at 140° and with copper at 160°.



Of the metals mentioned silver gives the best results, while iodo- and then bromo- give better yields than chloro-acids.

This synthesis has one rather anomalous application, when $\alpha$-bromo-isobutyric acid (or its ethyl ester) is heated with silver, some tetramethyl-succinic acid is produced in the ordinary way (B., 23, 297; 26, 1458). But there also appears trimethylglutaric acid (A., 292, 220). To explain the unexpected formation of this acid, it has been assumed that a portion of the $\alpha$-bromoisobutyric acid gives up HBr to form methylacrylic acid. This latter then forms $\beta$-bromoisobutyric acid, and the silver withdraws bromine from the $\alpha$- and $\beta$ acids, whereby the residues unite to tri-methyl-glutaric acid (B., 22, 48, 60). A similar explanation applies to some other syntheses in which tetramethylsuccinic and trimethylglutaric acids appear together.



Trimethylglutaric Acid.

(Compare this reaction with Reaction XLVII.)

**Reaction XXXVIII.** (*a*) **Action of Aqueous and Alcoholic Potassium or Sodium Cyanide on Aliphatic Halogen Compounds, and Hydrolysis of the Nitriles so formed.** (B., 14, 1965; 15, 2318.)—The preparation and hydrolysis of nitriles are dealt with on p. 151 and p. 239 respectively. In many cases, however, it is unnecessary to isolate the nitrile; it can be directly hydrolysed to the corresponding acid on its formation. Among others, the following syntheses have been carried out in this way:—

(i.) $n$-Valeric acid [*pentan acid*] from $n$-butyl bromide (Am. Soc., 42, 310).

(ii.) Methyl succinic acid [*methylbutan di-acid*] from propylene dibromide.

(iii.) *n*-Pimelic acid [*heptan di-acid*] from penta-methylene di-bromide.

(iv.) Tricarballylic acid [3-*carboxy-pentan di-acid*] from propenyl tribromide (Preparation 62).

(v.) Citric acid [3-*hydroxy*-3-*carboxy-pentan di-acid*] from dichloroacetonic acid.

PREPARATION 60.—**Malonic Acid** [*Propan di-acid*].

$$CH_2(COOH)_2. \qquad C_3H_4O_4. \qquad 104.$$

100 gms. (1 mol.) of powdered chloracetic acid are treated with 150 gms. of broken ice and dissolved in 125 gms. (1 mol.) of $33\frac{1}{3}\%$ caustic soda solution. If the liquid is still acid, it is exactly neutralised with caustic soda solution, and then treated with a solution of 69 gms. (1 mol.) of 98% potassium cyanide in 130 gms. of water which has been warmed to 40°. After an hour, the mixture is slowly warmed to 100° and kept at this temperature for 1 hour. It is allowed to cool to 25°, 125 gms. (1 mol.) of $33\frac{1}{3}\%$ caustic soda solution are again added, and the liquid is slowly warmed to 100° and kept at that temperature until no more ammonia is evolved (2—3 hours). When a sample of the liquid treated with more sodium hydrate solution gives no further ammonia on boiling, the conversion of the cyanoacetic acid into malonic acid is complete. The solution is cooled, acidified with dilute hydrochloric acid and carefully evaporated to complete dryness on a water bath. The residue is powdered and repeatedly extracted with ether and the ether removed on a water bath when malonic acid remains. It may be purified by dissolving in just sufficient caustic soda solution, boiling with animal charcoal, acidifying, evaporating to dryness, and extracting with ether as before.

$$CH_2Cl.COOH \xrightarrow{NaOH} CH_2Cl.COONa \xrightarrow{NaCN} CH_2(CN)COONa$$

$$\xrightarrow{NaOH} CH_2(COONa)_2 \xrightarrow{HCl} CH_2(COOH)_2.$$

*Yield*.—84% theoretical (95 gms.). Colourless crystals; easily soluble in water, alcohol, and ether; M.P. 132°; loses carbon dioxide yielding acetic acid at 140°—150°. All malonic acid homologues react similarly (see Reaction XXXIII. (*b*)). (A., 204, 125; B., 22, [2], 400.)

Diethyl malonate may be prepared from chloroacetic acid by a similar method.

PREPARATION 61.—**Succinic Acid** [*Butan di-acid*].

$$COOH.CH_2.CH_2.COOH. \qquad C_4H_6O_4. \qquad 118.$$

100 gms. (1 mol.) of ethylene dibromide and 75 gms. (excess) of potassium cyanide in alcoholic solution are refluxed on a water bath in a 750-c.c. round-bottomed flask until potassium bromide ceases to separate out from the solution. The latter is then cooled and filtered; 60 gms. (2 mols.) of solid caustic potash are added, and the mixture again refluxed on a water bath in a fume cupboard until the strong evolution of ammonia gas begins

to slacken. The flask is then cooled, and the contents are acidified with dilute hydrochloric acid and carefully evaporated to dryness. The dry powdered residue is repeatedly extracted with absolute alcohol, and the extract distilled on a water bath. The succinic acid remains behind in small crystals; it is recrystallised from hot water, decolorising if necessary with a little animal charcoal.

$$CH_2Br.CH_2Br + 2KCN = CH_2(CN).CH_2.CN + 2KBr.$$
$$(CH_2CN)_2 + 2KOH + 2H_2O = (CH_2COOK)_2 + 2NH_3.$$
$$(CH_2COOK)_2 + 2HCl = \begin{array}{l} CH_2.COOH \\ \mid \\ CH_2.COOH \end{array} + 2KCl$$

*Yield.*—80% theoretical (50 gms.). Colourless prisms; soluble in water, alcohol, and ether; insoluble in chloroform; sublime above 100° without decomposition; M.P. 185°; at 235° decompose forming the anhydride. (P. R. S., 10, 574; A., 120, 268.) For the isolation of ethylene dicyanide, see p. 151.

PREPARATION 62.—**Tricarballylic Acid** [3-*Carboxy-pentan-di-acid*].

$$\begin{array}{l} CH_2.COOH. \\ \mid \\ CH.COOH. \\ \mid \\ CH_2.COOH. \end{array} \qquad C_6H_8O_6. \qquad 176.$$

50 gms. (1 mol.) of glyceryl tribromide are dissolved in excess of alcohol, 36 gms. (1 mol.) of coarsely powdered potassium cyanide are added, and the whole heated for 15 hours in a soda-water bottle with the cork well tied down, in a water bath, the bottle being well wrapped in a cloth. A small autoclave can also be used. The bottle is then cooled in a freezing mixture, *carefully* (use goggles) opened, and the alcoholic liquid filtered from the potassium bromide which has separated out.

The filtrate is now refluxed on a water bath with a sufficient quantity (40 gms.) of caustic potash, to decompose the cyanide formed, until no more ammonia is evolved. The alcohol is distilled off on a brine bath, and the cooled residue evaporated to dryness with excess nitric acid. From it, after being well dried and powdered, the tricarballylic acid may be extracted with absolute alcohol. The dark-coloured substance obtained on evaporating off the alcohol is recrystallised from hot water with the addition of animal charcoal.

$$C_3H_5Br_3 + 3KCN = C_3H_5(CN)_3 + 3KBr.$$
$$CH_2(CN).CH(CN).CH_2CN + 3KOH + 3H_2O =$$
$$CH_2(COOH).CH(COOH).CH_2COOH + 3NH_3.$$

*Yield.*—70% theoretical (22 gms.). Colourless rhombic plates; easily soluble in water and alcohol; M.P. 161°. (P. R. S., 14, 77; O. S., X., 114.)

*General Methods of isolating organic acids from their salts* may here be noted.

(i.) An insoluble acid can be precipitated from a solution of a soluble salt by addition of dilute hydrochloric, sulphuric, or nitric acid, and

filtered off or extracted with a solvent (see Preparations 49, 54, 58, 189).

(ii.) A volatile acid soluble in water can be obtained by treatment of a solution of its alkali salt with sulphuric acid, dilute or strong, according as the acid is more or less volatile, and subsequent distillation (see Preparations 55, 178).

(iii.) A liquid or volatile acid soluble in water may be isolated by treatment of the lead salt with $H_2S$ and filtration or evaporation of the acid as it is liberated (see Preparation 191).

(iv.) A soluble non-volatile acid may be obtained by evaporating a soluble salt with dilute hydrochloric or nitric acids to dryness, and extracting the residue with a suitable solvent. Hydrochloric acid is usually preferable, as nitric acid may oxidise the product (see Preparations 60, 61, 62).

(v.) If the metal present be not an alkali metal, and if the acid be soluble, the former may be precipitated by addition of the exact quantity of sulphuric acid, say, or by means of $H_2S$ or hydrochloric acid; the filtrate is then evaporated to dryness or distilled. Sulphuric acid is used when calcium, strontium, barium, lead, etc., are present; hydrochloric acid when silver, lead, or mercury (-ous) are the metals to be dealt with; while $H_2S$ is advantageous when tin or lead have to be removed (see Preparations 64, 488, etc.). It is best to use sulphuric acid where a subsequent distillation is necessary.

**Reaction XXXVIII.** (*b*) **Action at 200° of Aqueous or Aqueous-alcoholic Potassium Cyanide in presence of Cuprous Cyanide on Aromatic Halogen Compounds, and Hydrolysis of the Nitriles so formed.** (B., 52, [B], 1749.)—It is difficult directly to replace nuclear halogen atoms in aromatic compounds, unless these atoms are rendered labile by the presence of nitro- or other negative groups (see p. 200). Lately, however, it has been shown that by the action of aqueous or aqueous-alcoholic potassium cyanide at 200°, using cuprous cyanide as catalyst, combined replacement of the halogen by CN and hydrolysis of the nitrile so formed occurs. In this way bromo-benzene has been directly converted into benzoic acid, *p*-dibromobenzene into terephthalic acid, and *p*-bromoaniline into *p*-aminobenzoic acid. Similar transformations have also been effected with derivatives of naphthalene and thiophen. For the action of copper powder on aromatic halogen compounds, see Reactions VII. (*b*) and LII. (*a*).

**Reaction XXXVIII.** (*c*) **Action of Hydrogen Cyanide on Aldehydes and Ketones and Hydrolysis of the Cyanohydrins so formed.** (B., 14, 235; C. Z., (1896), 90; C., (1900), I., 402.)—As is explained under Reaction L, aliphatic and aromatic aldehydes and ketones or their bisulphite compounds react with hydrogen cyanide to form cyanohydrins (α-hydroxy-nitriles). These are readily hydrolysed to α-hydroxy-acids, for the preparation of which the above reaction is often directly used since the isolation of the nitrile is unnecessary.

In the sugar group it is of especial interest, not only for its value in

determining constitution, but also for the synthesis of sugar and other derivatives containing long carbon chains. Thus *d*-glucose yields in this way the lactone of α-*d*-glucoheptonic acid, which may be reduced to α-*d*-glucoheptose—that is to a sugar containing one more secondary-alcohol group than the original sugar (see Reaction LXV. (*b*), where the subject is further treated).

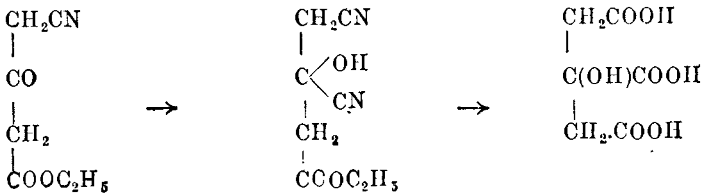
In this way, too, lactic acid has been synthesised from acetaldehyde.

$$CH_3CHO + HCN \rightarrow CH_3.CH(OH)CN \rightarrow CH_3CH(OH)COOH.$$

Dichloroacetonic acid has been prepared from dichloroacetone.

$$\begin{array}{c} CH_2Cl \\ | \\ CO \\ | \\ CH_2Cl \end{array} \quad \rightarrow \quad \begin{array}{l} CH_2Cl \\ | \\ C(OH)COOH \\ | \\ CH_2Cl \end{array}$$

while citric acid has been obtained from γ-cyano-aceto-acetate.



PREPARATION 63.—**Glycollic Acid** [*Ethanol Acid*].

$$CH_2(OH)COOH. \qquad C_2H_4O_3. \qquad 76.$$

20 gms. (1 mol.) of potassium cyanide (98%) are powdered and dissolved in 100 c.cs. of water, 26 c.cs. (1 mol.) of 40% formaldehyde are added, the mixture warmed—not above 30°—until homogeneous, and after standing 1 hour, treated slowly in a *good* draught cupboard with cold dilute hydrochloric acid (2 mols. ; 64 c.cs. conc. acid in 100 c.cs. of water), the whole being well stirred during the addition. Any hydrogen cyanide remaining is expelled by boiling (*caution !*) and the solution evaporated to dryness on a water bath. The powdered residue is extracted in a reflux apparatus with 50 c.cs. of boiling acetone and the filtered extract evaporated to dryness on a bath kept at 65°.

$$H.CH : O + KCN + 2H_2O = HCH(OH).COOK + NH_3.$$
$$CH_2(OH).COOK + HCl = CH_2(OH).COOH + KCl.$$

*Yield.*—70% theoretical (16 gms.). Colourless deliquescent crystals ; soluble in water and in acetone ; M.P. 80° ; K = 152. (B., 14, 1965 ; 15, 2318 ; C., (1900), I., 402.)

PREPARATION 64.—**α-*d*-Glucoheptonic Acid** [*Hepan*-2 : 3 : 4 : 5 : 6 : 7-*hexol-acid*].

$$CH_2OH.(CHOH)_5.COOH. \qquad C_7H_{14}O_8. \qquad 226.$$

100 gms. (1 mol.) of anhydrous grape-sugar are dissolved in 500 c.cs. (1 mol. of HCN) of 3% hydrocyanic acid (*caution !*) and treated with 10

drops of dilute ammonia. The mixture is allowed to stand for 4—5 days in a fume cupboard at room temperature, and is then treated with a solution of 130 gms. (excess) of barium hydrate in 400 c.cs. of water and boiled in a dish in a fume cupboard until the smell of ammonia has disappeared.

The liquid is now acidified with dilute sulphuric acid; the hydrocyanic acid is driven off by boiling in a fume chamber (*caution !*) and the sulphuric acid exactly precipitated with strong baryta-water. After boiling with animal charcoal, the solution is filtered and evaporated to a syrup on a water bath. On long standing, the lactone of $\alpha$-*d*-glucoheptonic acid separates in crystals. These are macerated with a little 80% alcohol, and filtered at the pump. The substance is then dissolved in 3 times its weight of water, and treated with animal charcoal in the warm. The filtrate is concentrated and set aside to crystallise.

$$CH_2OH(CHOH)_5CHO \rightarrow CH_2(OH)(CHOH)_5CH(OH)CN \rightarrow$$
$$CH_2OH.(CHOH)_5.CHOH.COOH.$$

*Yield.*—70% theoretical (90 gms.). Colourless crystals; soluble in water; M.P. 140°. (B., 19, 1916; 23, 936; A., 270, 65, 272, 200.)

It is noteworthy that it is often preferable to use the bisulphite compound of the aldehyde rather than the aldehyde itself (see p. 156). The small quantity of ammonia used above to help the reaction may do so by the momentary formation of the ammonia compound of the aldehyde.

$$\overset{|}{C}HO + NH_3 \rightarrow H\overset{|}{C}\begin{matrix} \diagup OH \\ \diagdown NH_2 \end{matrix}$$

$$H\overset{|}{C}\begin{matrix} \diagup OH \\ \diagdown NH_2 \end{matrix} + HCN \rightarrow H\overset{|}{C}\begin{matrix} \diagup OH \\ \diagdown CN \end{matrix} + NH_3.$$

Hydrogen cyanide seems to react in this way more readily than it unites directly to the carbonyl group.

$$\overset{|}{C}HO + HCN \rightarrow \overset{|}{C}H\begin{matrix} \diagup OH \\ \diagdown CN. \end{matrix}$$

The lactone of $\alpha$-*d*-fructose-carboxylic acid, M.P. 130°, is prepared in the same manner from *d*-fructose (lævulose). It will be noted that from glucose, four carboxylic acids can be obtained—an $\alpha$- and $\beta$-acid from each of the optical isomers (A., 270, 64). Like many acids containing a $\gamma$-hydroxy group, all these free acids are unstable, immediately forming lactones on liberation from their salts.

**Reaction XXXIX. Fusion of the Salts of Aromatic Sulphonic Acids with Sodium Cyanide or with Sodium Formate.**—These are important reactions which result in the formation of nitriles and carboxylic acids.

$$R.SO_3Na + NaCN = R.CN + Na_2SO_3$$
$$R.SO_3Na + HCOONa = R.COONa + NaHSO_3.$$

Nitriles are converted by hydrolysis into carboxylic acids (see Reaction XXXVIII.), so that the former reaction affords a convenient method of synthesising aromatic carboxylic acids.

**Reaction XL.** (*a*) **Condensation of a Phenol with a "Methane Carbon Atom."** (A., 194, 123; 196, 77; B., 28, R., 743.)—Phenols can be condensed with compounds which can yield a nuclear carbon, to give dyes of the rosolic acid series. The *leuco*-compound—tri-hydroxytriphenyl carbinol—first formed, is unstable and immediately yields the dyestuff, no oxidising agent being necessary. In this respect these compounds differ from the analogous rosaniline compounds (see p. 382).

Aurin, the simplest member of the series, is prepared by heating together phenol, oxalic, and strong sulphuric acids at 130° for 6 hours.

$$(\mathrm{COOH})_2 \xrightarrow{\mathrm{H_2SO_4}} \mathrm{C}\begin{matrix}{/\!\!/}\mathrm{O}\\ {\backslash\!\!\backslash}\mathrm{O}\end{matrix} \quad (+\,\mathrm{CO}) \xrightarrow{2\mathrm{C_6H_5OH}}$$

$$\mathrm{C}\begin{matrix}{/\!\!/}(\mathrm{C_6H_4OH})_2\\ {\backslash\!\!\backslash}\mathrm{O}\end{matrix} \xrightarrow{\mathrm{C_6H_5OH}} \left[\begin{matrix}\mathrm{C}\equiv(\mathrm{C_6H_4OH})_3\\ |\\ \mathrm{OH}\end{matrix}\right] \rightarrow$$

$$(\mathrm{HOC_6H_4})_2 = \mathrm{C} = \mathrm{C_6H_4} = \mathrm{O}.$$

The methane carbon atom can also be supplied by formaldehyde; the steps in the synthesis are—

$$\mathrm{H_2C{=}O} + \begin{matrix}\mathrm{H.C_6H_4.OH}\\ \mathrm{H.C_6H_4.OH}\end{matrix} \rightarrow \mathrm{H_2C(C_6H_4OH)_2} \xrightarrow{\mathrm{C_6H_5OH}\ +\ \mathrm{O}}$$

$$\left[\begin{matrix}\mathrm{C(C_6H_4OH)_3}\\ |\\ \mathrm{OH}\end{matrix}\right] \rightarrow (\mathrm{HOC_6H_4})_2\mathrm{C} = \mathrm{C_6H_4} = \mathrm{O}.$$

Rosolic acid (methyl aurin), another important member of this series, is prepared by oxidising a mixture of phenol and *o*- and *p*-cresols with arsenic acid and sulphuric acid. 1 mol. of each of the cresols and 1 mol. of phenol react, the methyl carbon of the *p*-cresol molecule serving as a nuclear carbon.

These compounds dissolve in alkalis, and alcohols with a bright red colour, but they are now little used as dyes. As will be seen, they are assumed to have a quinonoid formula like all the triphenylmethane dyes (see p. 381).

**Reaction XL.** (*b*) **Action of Carbon Monoxide on Alcohols under pressure in Presence of Catalysis.** (J. C. S., 1936, 358.)—Acetic acid and higher acids can be formed by the action of carbon monoxide on the alcohol at 330° and 200 atm. in presence of phosphoric acid catalysts. Branched chain acids may be formed from normal alcohols, through the intermediary of the olefines derived from the alcohols by dehydration.

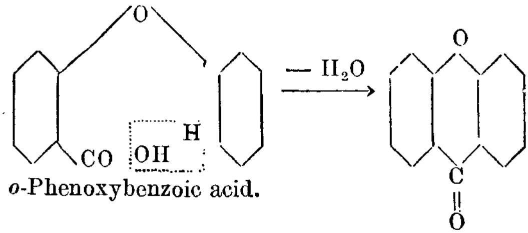
# CHAPTER VII

## CARBON TO CARBON

### Oxide-Oxy Compounds

In this section those nuclear syntheses of which the product is necessarily an ester or some other compound containing both an oxy (carbonyl) and an oxide (ether) group are described. Many important reactions are here involved—partly owing to the activating influence of the carbonyl group, and partly because the inertness of the oxide group enables carbonyl compounds containing it to be used, where the corresponding hydroxy-oxy compound (acid) is inadmissible, owing to the reactivity of its hydroxyl group. On this account, these ester syntheses are often only undertaken to obtain an acid by an after-hydrolysis.

**Reaction XLI. Elimination of Water from *o*-Phenoxybenzoic Acids (*o*-Phenylsalicylic Acids).** (B., 21, 502; 25, 1652; 26, 71.)—The xanthones (di-benzpyrones) possess a chromogenic nature, and form the basis of some dyestuffs. They are obtained by loss of water from the *o*-phenoxybenzoic acids by treating the latter with dehydrating agents—conc. sulphuric acid at 100°, fused zinc chloride, or acetic anhydride.



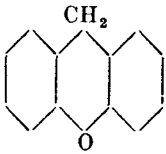
*o*-Phenoxybenzoic acid. Xanthone.

They have also been synthesised by condensing salicylic acid with phenols through the agency of sulphuric acid, acetic anhydride, etc. (B., 21, 502; 24, 3982; 25, 1652; 26, 71; 27, 1989; A., 254, 265). All four possible mono-hydroxyxanthones have been prepared in this way, as have some of the poly-hydroxy compounds. These latter are the more important.

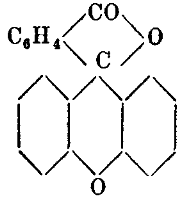
$$(HO)C_6H_3\begin{matrix}\diagup H\\ \diagdown OH\end{matrix} + \begin{matrix}OH.CO\diagdown\\ OH\diagup\end{matrix}C_6H_4 \rightarrow HOC_6H_3\begin{matrix}\diagup CO\diagdown\\ \diagdown O\diagup\end{matrix}C_6H_4.$$

The xanthones are allied to the thio-xanthones (J. C. S., 97, 1290), the acridones (B., 25, 1734) and the fluorones (J. C. S., 99, 545). The mother

substance obtained by reduction of xanthone is xanthene (methylene-diphenylene oxide). (B., 26, 72.)



Xanthene.



Fluorane.

Although the xanthones contain a ketone oxygen atom, they, like the pyrones (see p. 385), do not react with hydroxylamine, or phenyl hydrazine.

**Reaction XLII. Prolonged action of Heat on Ethyl Acetoacetate.** (A., 273, 186.)—By prolonged boiling of acetoacetic ester under a reflux condenser at ordinary pressures, condensation occurs, and dehydracetic acid is formed. The parent acid, a δ-hydroxy-acid, is unstable, and has not yet been isolated.

$$\begin{array}{ll} \quad CO.OC_2H_5 & \quad HO.C.CH_3 \\ \quad\;| & \qquad\quad \| \\ CH_3.CO.CH_2 & C_2H_5O.CO.CH \end{array} \longrightarrow \begin{array}{l} \quad CO—O——C.CH_3 \\ \quad\;| \qquad\qquad\;\; \| \\ CH_3.CO.CH—CO—CH \end{array} + 2C_2H_5OH.$$

1 mol. of the keto reacts with 1 mol. of the enol form ; it will be noted how the activated methylene group enters into the reaction.

The lactone formed is important because hydriodic acid reduces it to di-methyl pyrone $CH_3\overset{|\!\!-\!\!-\!\!-O-\!\!-\!\!-|}{C:CH.CO.CH:C}.CH_3$, a certain amount of rearrangement occurring. This latter compound is, like all the pyrones, of great theoretical interest (see p. 106). Also dehydracetic acid figures in the chemistry of the ketenes, ketene itself polymerising to it, under the influence of zinc bromide or tertiary amines, or even spontaneously.

$$CH_2{=}CO \quad \begin{array}{c} CO \\ \| \\ CH_2 \end{array} \quad \begin{array}{l} OC = CH_2 \\ \\ OC = CH_2 \end{array} \xrightarrow{(C_2H_5)_3N} \begin{array}{l} \quad CO—O—C.CH_3 \\ \quad\;| \qquad\quad\;\; \| \\ CH_3.CO.CH—CO—CH. \end{array}$$

(A., 273, 186 ; C., 1900, II., 625 ; A., 257, 261.)

PREPARATION 65.—**Dehydracetic Acid** (*Methylacetopyronone*).

$$\begin{array}{l} \quad CO — O — C.CH_3. \\ \quad\;| \qquad\qquad\;\; \| \\ CH_3.CO.CH—CO—CH \end{array} \qquad C_8H_8O_4. \qquad 168.$$

20 gms. (2 mols.) of ethyl acetoacetate are boiled under a reflux for 6 hours, pieces of porous porcelain being added to promote regular ebullition. The liquid is then distilled to 200° ; the distillate may be fractionated *in vacuo* to recover unchanged acetoacetic ester (see Preparation 75). The brown residue solidifies on cooling to a crystalline mass. It is boiled with 5N caustic soda solution with the addition of animal charcoal and filtered

hot. The sodium salt crystallises from the filtrate; acidification with dilute sulphuric acid precipitates the required lactone.

$$2CH_3.CO.CH_2COOC_2H_5 = C_8H_8O_4 + 2C_2H_5OH.$$

*Yield.*—80% theoretical, allowing for acetoacetic ester recovered (10 gms.). Colourless needles; insoluble in water; M.P. 108°; B.P. $^{760}$ 269°; K = 0·00053. (A., 257, 261; B., 27, R., 417.)

**Reaction XLIII.** (*a*) **Formation of Esters by the action of Acid Anhydrides or of Acid Chlorides on an Alcohol in the presence of Magnesium Alkyl Halide** (Grignard). (B., 39, 1738.)—This application of the Grignard reaction to the preparation of esters is of theoretical rather than practical interest as illustrating the wide applicability of this many-sided reaction. The steps in the synthesis will be clear from the examples given; they are somewhat different from the usual phases of a Grignard reaction.

$$\text{(i.)}\ RMgI + (CH_3)_3C(OH) = (CH_3)_3COMgI + R.H.$$

$$2(CH_3)_3COMgI + (CH_3CO)_2O \longrightarrow$$

$$\begin{array}{l} \quad\ \ /OMgI \\ CH_3.C-O.C(CH_3)_3 \\ \quad\ \ \backslash O \\ \quad\ \ / \\ CH_3.C-OC(CH_3)_3 \\ \quad\ \ \backslash OMgI \end{array} \xrightarrow{H_2O} 2CH_3.CO.O.C.(CH_3)_3 + (IMg)_2O.$$

$$\text{(ii.)}\ (CH_3)_3COMgI + CH_3COCl = CH_3CO.O.C(CH_3)_3 + MgClI.$$

Iso-amyl acetate has been obtained in this way from isoamyl alcohol and acetyl chloride. The method does not offer any advantages over the more usual esterification reactions.

For the general experimental method and precautions necessary in Grignard reactions, see Preparation 19.

**Reaction XLIII.** (*b*) **Formation of Ethyl Esters by the Action of Ethyl Chloroformate on Magnesium Alkyl Halide in Dry Ethereal Solution** (Grignard).—This is another mode of application of the Grignard reaction to the synthesis of esters. It is more direct than the previous method.

$$CH_3Mg.Cl + Cl.COOC_2H_5 \longrightarrow \begin{array}{l} \quad /OMgCl \\ Cl.C.OC_2H_5 \\ \quad \backslash CH_3 \end{array} \longrightarrow CH_3.COOC_2H_5 + MgCl_2.$$

**Reaction XLIII.** (*c*) **Condensation of $\alpha$-Halogen Fatty Acid Esters with Aldehydes and Ketones by means of Zinc or Magnesium** (Reformatsky-Grignard). (C., (1901), I., 1196; II., 30; (1902), I., 856.)—This is an extension of the Grignard and zinc alkyl reactions which enables $\alpha$-halogen esters to be condensed with carbonyl compounds as if they were simple alkyl halogen compounds. The zinc or magnesium alkyl derivative is neither prepared beforehand nor isolated in the reaction, but there is little doubt that some such compound is transitorily formed. Zinc is the metal

most usually employed. The product is a β-hydroxy ester, and the method is the standard one for obtaining the higher β-hydroxy acids. The equation below illustrates this :—

$$CH_3.CHBr.COOC_2H_5 + Zn \rightarrow CH_3\overset{\overset{ZnBr}{|}}{C}H(COOC_2H_5).$$

$$CH_3.CHO + CH_3.\overset{\overset{ZnBr}{|}}{C}H(COOC_2H_5) \rightarrow$$

$$CH_3.CH(\overset{\overset{OZnBr}{|}}{C}HCH_3).COOC_2H_5 \xrightarrow{H_2O}$$

$$CH_3CH(\overset{\overset{OH}{|}}{C}H.CH_3).COOC_2H_5$$

Preparation 66.—**Ethyl β-hydroxy-αβ-dimethylbutyrate** [*Ethyl ester of 2 : 3-dimethyl-3-butanol acid*].

$$\left.\begin{matrix}CH_3\\CH_3\end{matrix}\right> C(OH).CH(CH_3).COOC_2H_5 \qquad C_8H_{16}O_3. \qquad 160.$$

60 gms. of zinc are freed from oxide and oil by washing successively with warm caustic soda solution, then dilute acid, water and alcohol. After being dried in an air oven, a small quantity is added to a mixture of 90 gms. pure dry acetone and 182 gms. of ethyl-α-bromopropionate contained in a large flask provided with a reflux condenser. The flask is gradually warmed on a water bath until a reaction commences, and if it proceeds too vigorously, cooling must be applied. More zinc is added from time to time as the action subsides, until some of the metal remains undissolved (about 45 gms. Zn are usually required), and after the final addition, heating is continued for 2—3 hours. The syrupy liquid is poured off from the unattacked metal, and water added. The basic zinc bromide which is precipitated is dissolved by the addition of a sufficient quantity of dilute sulphuric acid, and the oily layer is extracted with ether and separated. The extract is washed three times with dilute sulphuric acid, then with water, and dried over calcium chloride. After the ether is removed, the residue is distilled at 30 mms. pressure, when the pure ester passes over about 105°.

$$CH_3CHBrCOOC_2H_5 + Zn \rightarrow BrZn - CH(CH_3)COOC_2H_5.$$

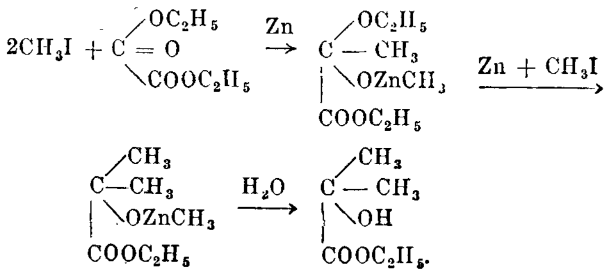
$$\begin{array}{c}CH_3\\|\\CO\\|\\CH_3\end{array} + BrZnCH(CH_3)COOC_2H_5 \rightarrow \begin{array}{c}CH_3\\|\\C\\|\\CH_3\end{array}\!\!\begin{array}{l}\diagup OZnBr\\ \\ \diagdown CHCH_3.COOC_2H_5\end{array}$$

$$\xrightarrow{H_2O} CH_3C(OH)(CH_3)CH(CH_3)COOC_2H_5.$$

$Zn[CH(CH_3)COOC_2H_5]_2$ might also be considered an intermediate compound in the reaction.

*Yield.*—50% theoretical (60 gms.). Colourless oil, insoluble in water; B.P. $^{30}$, 105°. (C., (1901), I., 1196; II., 30; (1902), I., 856.)

**Reaction XLIII.** (*d*) **Condensation of Diethyl Oxalate with Alkyl Halides in the presence of Zinc** (Frankland--Duppa). (A., 185, 184.)—This is a type of condensation very similar to those just described. The zinc alkyl is not isolated, and simple halogen compounds are used. The product is a derivative of glycollic acid.



**Reaction XLIV.** (*a*) **Condensation of Alkyl and Acyl Halides with Ethyl Sodio-malonate and its Homologues.** (B., 7, 1383; Am. Soc., 43, 680.)—The malonic esters are almost as valuable as the acetoacetic esters (see Reaction XLIV. (*b*) ) in the syntheses of mono- and poly-carboxylic acids owing to the successive replaceability by sodium of the hydrogen atoms of the methylene group, activated as it is by two neighbouring carbonyl groups. These sodio-derivatives are very reactive, and undergo the following changes:—

(i.) By the action of alkyl halide on the sodio compound, a mono-alkyl compound is formed.

$$CH_2(COOC_2H_5)_2 \xrightarrow{Na} CHNa(COOC_2H_5)_2 \xrightarrow{RI} CHR(COOC_2H_5)_2.$$

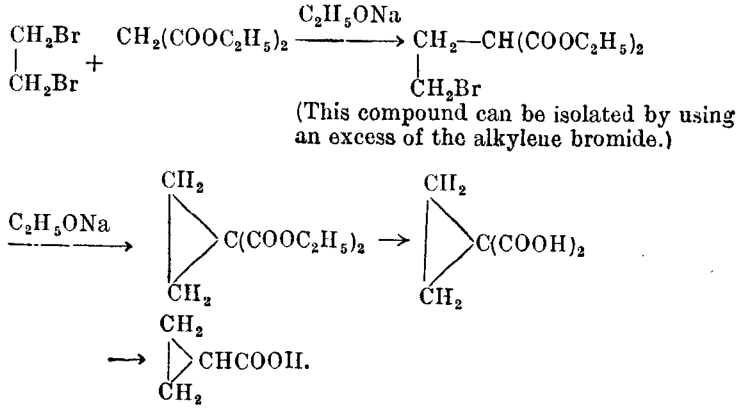
(ii.) By the action of alkyl halide on the sodio-derivative of a mono-alkyl malonic ester, a di-alkyl compound is produced.

$$CHR(COOC_2H_5)_2 \xrightarrow{Na} CNaR(COOC_2H_5)_2 \xrightarrow{R_1I} CR_1R(COOC_2H_5)_2.$$

From these esters the corresponding dibasic acids can be obtained by hydrolysis, so that the homologues of malonic acid can be synthesised in this way.

Again, as all these acids have two carboxyls attached to the same carbon atom, they lose carbon dioxide on heating and pass into mono-basic fatty acids (B., 27, 1177). This affords an important and standard synthesis for these latter acids (see Preparation 427, also Preparation 60 and p. 113).

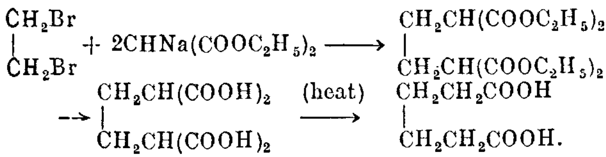
(iii.) Cyclo paraffin derivatives can also be synthesised. Malonic ester and ethylene bromide in the presence of sodium alcoholate yield tri-methylene-di-carboxylic ester and thence a di- and mono-carboxylic acid. (Am. Soc., 42, 314; 43, 680.)



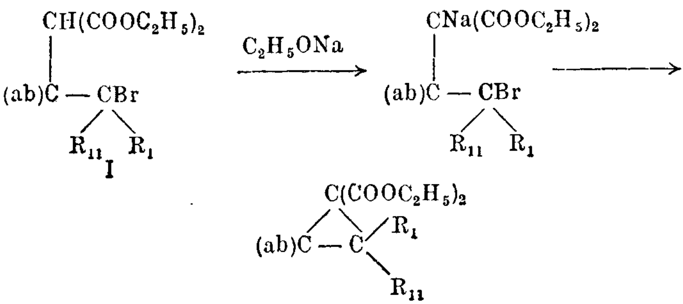

$C_2H_5ONa$ s more frequently used to obtain the sodio-derivatives of the malonic esters, though metallic sodium can also be employed.

By using various alkylene dibromides, 4, 5, 6 or 7 membered rings can also be obtained. (A., 284, 197.)

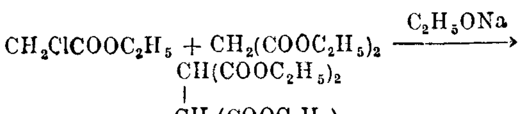
(iv.) Simultaneously there is formed in the above reaction butane-tetra-carboxylic ester, and it yields a tetra- and thence a dibasic acid (adipic acid). The tetra-basic ester can also yield ring compounds (Reaction XLVII.).



(v.) Also by starting with compounds such as I., ring compounds may be synthesised by intra-molecular condensation.



(vi.) Halogen esters react like simple alkyl halides.


Ethane-tricarboxylic Ester.

(vii.) The acyl malonic esters are produced from the acyl chlorides, and sodio-malonic ester in a manner exactly analogous to the alkyl malonic esters (B., 20, R., 381).

Benzoyl chloride, and sodio-ethyl malonate yield diethyl benzoylmalonate.

$$C_6H_5COCl + CHNa(COOC_2H_5)_2 \rightarrow (C_6H_5CO)CH(COOC_2H_5)_2.$$

The structure of the sodio-derivatives of diketomethylene compounds, like malonic ester, is dealt with in Reaction XLIV. (*b*), and an explanation is given as to why only one hydrogen is replaceable at a time.

PREPARATION 67.—**Diethyl Ethylmalonate.**

$$C_2H_5CH(COOC_2H_5)_2. \qquad C_9H_{16}O_4. \qquad 188.$$

To 25 gms. of absolute alcohol contained in a flask provided with a reflux condenser, 2·3 gms. of sodium are added, and when the metal has dissolved, 16 gms. of ethyl malonate are added. The sodio-derivative of the ester is precipitated as a white solid. The flask is shaken while 20 gms. of ethyl iodide are slowly run in from a dropping funnel; the precipitate gradually reacts and sodium iodide is deposited. Heating is conducted on a water bath (1—2 hours) until the product ceases to show an alkaline reaction. The alcohol is distilled off, the residue diluted with water and extracted with ether. The extract is dried over calcium chloride, the ether distilled off, and the residue fractionated, when the product passes over at 200°—210°.

$$CH_2(COOC_2H_5)_2 \rightarrow CHNa(COOC_2H_5)_2 \rightarrow C_2H_5.CH(COOC_2H_5)_2.$$

*Yield.*—75% theoretical (15 gms.). Colourless oil of fruity odour; B.P. 207°; D. $^{18}_{4}$ 1·008. (A., 204, 134.)

Methyl, propyl, butyl, etc., malonic esters are also obtained in a similar manner. It is to be observed that aryl halides do not undergo this reaction. The di-alkyl esters are obtained from the mono-alkyl esters in the same way as the latter are obtained from malonic ester. But although di-alkyl compounds are not formed directly in any quantity, yet it frequently happens that a little is obtained in the preparation of the mono-alkyl compound from 1 mol. of sodium ethoxide and 1 mol. of alkyl halide, owing to the mono-derivative reacting with more sodium and alkyl halide. This may be prevented when necessary by using only half the calculated quantity of sodium and alkyl halide. By this means the yield of benzoyl malonic ester for example is raised from 55% to 85% in its preparation from sodium, benzoyl chloride and malonic ester. (B., 44, 1507.)

**Reaction XLIV.** (*b*) **Condensation of Alkyl and Aryl Halogen Compounds with the Sodio- and other Metallo-derivatives of Ethyl Acetoacetate and its Homologues.** (A., 186, 214; 201, 143; 213, 143.)—Like malonic ester, acetoacetic ester contains two 1 : 3-carbonyl groups with a methylene group in position 2. It is only to be expected then that it yields with metallic sodium or sodium alcoholate sodio-derivatives from which mono- and di-, alkyl and aryl homologues can be obtained by treatment with a suitable halide, including halogen esters. Acetoacetic acid

shows the same property, but its great instability necessitates the use of its very stable ethyl ester. Other examples of 1 : 3 di-keto-2-methylene compounds, of which all possess similar properties to the esters described in this and the previous reaction, will be found on p. 97. Reference may also be made to Reaction XLVI.

These compounds are alike in being tautomeric, the keto and enol forms being in an equilibrium which varies both with substance and with temperature—

$$—CO.CH_2.CO— \rightleftarrows —C(OH):CH.CO—$$

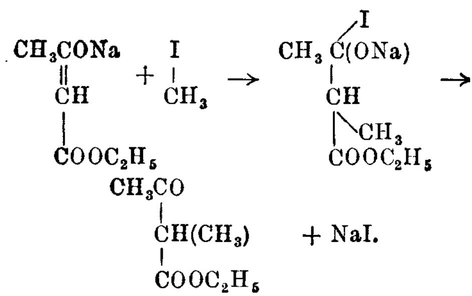
and

$$—CO.CHR.CO— \rightleftarrows —C(OH):CR.CO—$$

It is this equilibrium which renders difficult the explanation of the course of the reactions which take place when metallic sodium or sodium ethoxide and then alkyl or acyl halide are added to these compounds. At first it was thought that the sodio compound formed with acetoacetic ester was $CH_3.CO.CHNa.COOC_2H_5$, because the reaction with alkyl and acyl halides always yielded a C-derivative, $CH_3.CO.CHR.COOC_2H_5$. The first example of a different course of reaction was found in the formation of an O-derivative—$\beta$-carbethoxyhydroxycrotonic ester from sodioacetoacetic ester and chloroformic ester (J. pr., [2], 37, 473 ; B., 25, 1760 ; A., 277, 64). This could only be explained by assigning an enol formula to the sodium salt—

$$CH_3C(ONa):CHCOOC_2H_5 + ClCOOC_2H_5 \rightarrow CH_3.C(OCOOC_2H_5):CHCOOC_2H_5.$$

This immediately explained why only one of the methylene hydrogen atoms is replaceable at a time. The formation of C-derivatives could then be looked on as an addition reaction followed by the separation of sodium halide.

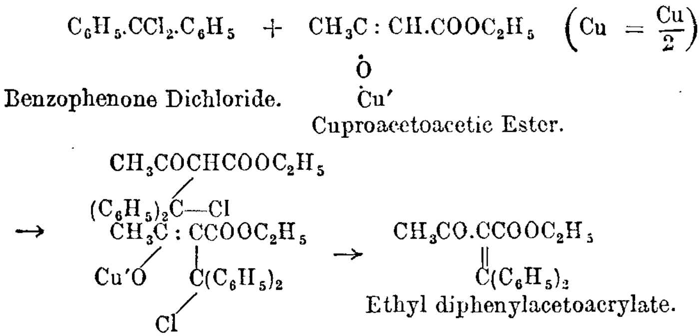


Some of the C-derivative, acetylmalonic ester, is also formed in the chloroformic ester condensation quoted above. In the majority of cases the C-derivative is produced to the exclusion of the O-derivative. For an explanation, see J. pr., [2], 37, 473 ; see also equation (4), p. 140.

The various alkyl derivatives of acetoacetic ester are important, because of the hydrolyses they undergo (see p. 193). Some reference to the structure of the acetoacetic ester will be found under Reaction XLVI., p. 145 ; further reactions are discussed in Reactions XLVII., LIII.

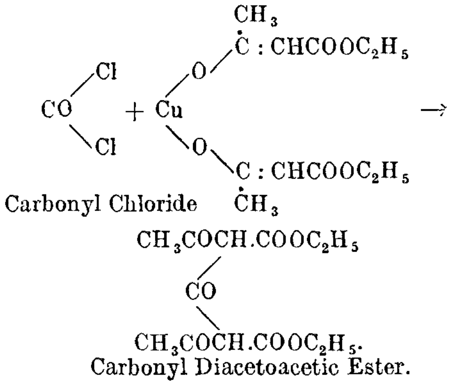
The following equations will illustrate some extensions of which the reaction is capable :—

(1)



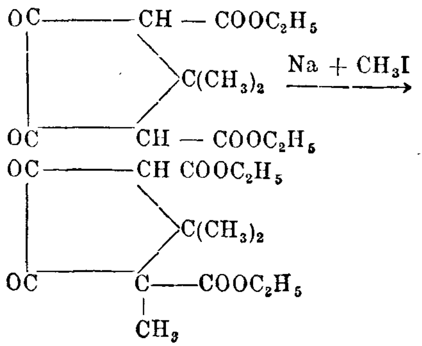

The reaction may be assumed to go as above. The copper derivative of acetoacetic ester is formed by adding a saturated alcoholic solution of cupric acetate to the ester; a bluish-green crystalline precipitate $(C_6H_9O_3)_2$ Cu is produced (*cf.* p. 98.)

(2)




The latter compound is important in the synthesis of $\gamma$-pyrone.

(3) Attention may also be drawn to the synthesis of ethyl diketocamphorate from ethyl diketocamphopyrate (see Reaction XLVI. (iii.) ).



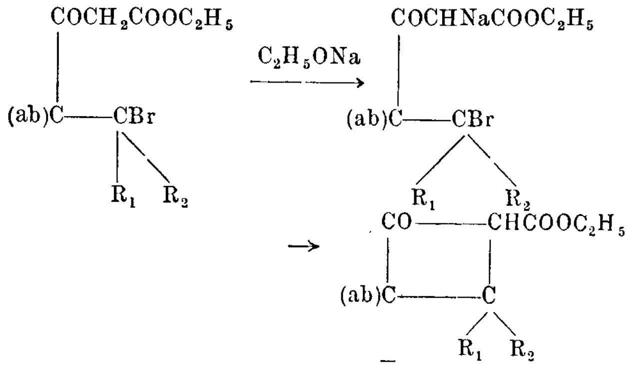
(4) It is of interest to note that while chloroformic ester yields mostly the O-derivative, it is only the C-derivative that is obtained from chloroacetic ester.

$$CH_2Cl.COOC_2H_5 + CH_3C(ONa):CHCOOC_2H_5 \rightarrow CH_3COCH(CH_2COOC_2H_5)COOC_2H_5.$$

Acetylsuccinic Ester.

On the other hand, chloroformic ester yields the C-derivative with cuproacetoacetic ester. (B., 37, 3394, 4627; 38, 22.)

(5) In the previous reaction (v.), ring compounds may be synthesised by intramolecular condensation.




The following preparations show the experimental methods used. It is to be noted that in all these reactions bromides and iodides give better yields than chlorides.

PREPARATION 68.—**Ethyl Ethylacetoacetate** [*Ethyl ester of* 2-*ethyl*-3-*on butan acid*].

$$CH_3.CO.CH(C_2H_5)COOC_2H_5. \qquad C_8H_{14}O_3. \qquad 158.$$

32·5 gms. (1 mol.) of ethyl acetoacetate are slowly added with cooling to the solution obtained by dissolving 5·7 gms. (1 atom) of clean sodium wire in 70 gms. of absolute alcohol under a reflux. 40 gms. (1 mol.) of ethyl iodide are then slowly added, and the whole refluxed on a water bath until it shows a neutral reaction. If necessary a little more ethyl iodide is added. The alcohol is removed on a water bath and the residual oil shaken with water and extracted with ether. The ethereal extract is dried over anhydrous potassium carbonate, the ether removed on a water bath, and the residue distilled, the portion boiling at 190°—198° at 760 mms. being collected separately. If preferred, the fractionation can be done under reduced pressure.

$$CH_3.CO.CH_2.COOEt \xrightarrow{C_2H_5ONa} CH_3.CO.CHNa.COOEt \xrightarrow{C_2H_5I} CH_3.CO.CH(C_2H_5)COOEt.$$

*Yield.*—80% theoretical (32 gms.). Colourless oil; insoluble in water; B.P. $^{14}$ 84°; B.P. $^{760}$ 198°; D. $^{16}_{4}$ 0·9834. (A., 186, 220; 192, 153; C., (1904), II., 309; A., 441, 153.)

Other mono-alkyl acetoacetic esters may be prepared in an exactly

analogous manner, using corresponding molecular quantities of the alkyl iodides.

In the preparation of some of the higher mono-alkyl acetoacetic esters the yield is sensibly lowered, owing to the formation of di-alkyl compounds due to secondary reactions of the same type as those described on p. 137. This in like manner can be remedied by using only half the calculated quantity of sodium and alkyl halide. The unattacked acetoacetic ester is recovered by distillation.

PREPARATION 69.—**Ethyl Benzylacetoacetate.**

$$CH_3COCH(CH_2C_6H_5)COOC_2H_5. \qquad C_{13}H_{16}O_3. \qquad 220.$$

To a solution of 6 gms. (1 atom) of sodium in 75 c.cs. (excess) of absolute alcohol are gradually added 65 gms. (2 mols.) of acetoacetic ester. 32 gms. benzyl chloride are dropped in, and the temperature of the mixture is maintained at 30° for an hour. It is then refluxed for an hour. The product is distilled under reduced pressure, the fraction 164°—165° at 14 mms. consisting of benzyl acetoacetic ester being retained. Up to this temperature the unattacked acetoacetic ester passes over.

$$CH_3COCHNaCOOC_2H_5 + C_6H_5CH_2Cl \rightarrow CH_3COCH(CH_2C_6H_5)COOC_2H_5.$$

*Yield.*—85% theoretical (47 gms.). Colourless oil; B.P. $^{14}$ 165°; B.P. $^{760}$ 276°; insoluble in water. (A., 204, 179.)

An equally good yield can be obtained by replacing the ethyl alcohol by 100 c.cs. butyl alcohol.

The di-alkyl esters are made from the mono-alkyl esters in a manner exactly similar to that by which the mono-alkyl esters are made from acetoacetic ester itself.

The method of preparation of acyl acetoacetic esters is exemplified in the following. The reaction goes through phases similar to those described for alkyl compounds, but owing to the greater reactivity of the acyl halides, special precautions have to be taken. Unlike the alkyl chlorides, the acyl chlorides give good yields; there is no need to use the bromides or the iodides.

PREPARATION 70.—**Ethyl Benzoylacetoacetate.**

$$\begin{array}{l} \quad\;\;\; COC_6H_5 \\ \qquad\;\, | \\ CH_3COCH.COOC_2H_5. \end{array} \qquad C_{13}H_{14}O_4. \qquad 234.$$

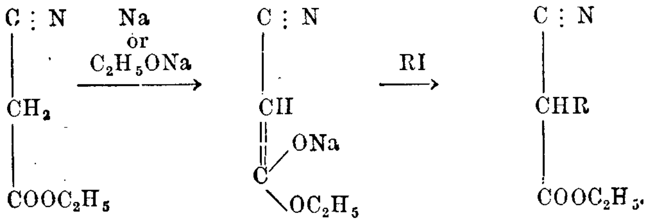
To 600 c.cs. of absolute alcohol in a flask attached to a reflux are gradually added 35 gms. (2 atoms) of sodium cut in small pieces. When all the sodium has dissolved, the solution is cooled. To 300 c.cs. of this solution are added 100 gms. (1 mol.) of acetoacetic ester, and, with continual stirring, 45 c.cs. of benzoyl chloride are dropped in from a burette during 15 minutes, the temperature being kept below 10°. After 30 minutes, 150 c.cs. of the original solution and 22 c.cs. benzoyl chloride are added as before. This process is repeated until all the original solution is used up, and 90 c.cs. benzoyl chloride in all. After 12 hours, the sodium salt is filtered off and washed with ether. By acidifying with dilute acetic

acid in presence of ice-water, the ester is liberated. It is extracted with ether, dried over anhydrous sodium sulphate, and the ether removed. The residue is then distilled under reduced pressure, the fraction 173°—177° at 12 mms. being retained.

$$CH_3CO.CHNaCOOC_2H_5 + C_6H_5COCl \rightarrow CH_3COCH(COC_6H_5)COOC_2H_5.$$

Viscous oil; insoluble in water; B.P. $^{12}$, 175°, with slight decomposition; tautomeric. (B., 18, 2131; 44, 1507.)

**Reaction XLIV.** (*c*) **Condensation of Alkyl and Acyl Halides with the Sodio-derivatives of Ethyl Cyanoacetate.** (B., 20, R., 477; 21, R., 353; 27, R., 262; J. pr., [2], 51, 186.)—Cyanoacetic, $\mathbf{CH_2(CN)COOC_2H_5}$, has similar properties to malonic and acetoacetic esters, inasmuch as the methylene hydrogen atoms are successively replaceable by sodium and this latter by alkyl and acyl radicals.



The activation of the methylene hydrogens is effected by the presence of **C : O** groups, as well as by other groups containing double and multiple linkings. This is somewhat analogous to the activating effect of nitro groups in aromatic compounds. Reference may also be made to the hydroxymethylene compounds, Reaction XXIII. (*a*).

The groups **C : O** and **C ⋮ N** resemble one another in many of their reactions. It may be noted that unsaturated groups always tend to give an acid character to any compound in which they occur.

The synthesis may be extended to halogen esters (*cf.* vi., p. 136).

$$CH_2ICOOC_2H_5 + CN.CH_2COOC_2H_5 \xrightarrow{C_2H_5ONA} \begin{matrix} CH_2COOC_2H_5. \\ CN.CH(COOC_2H_5) \end{matrix}$$

Cyanosuccinic Ester.

**Reaction XLV. Condensation of Aldehydes and Ketones with certain Esters under the influence of Acetic Anhydride, Hydrochloric Acid, Sodium Ethoxide or certain bases.** (A., 218, 172; B., 29, 172; 30, 481; 31, 735, 2585.)—1 mol. of an aldehyde can be made to condense with 1 mol. of an ester containing an $\alpha$-methylene group, thus

$$R_1CHO + RCH_2COOC_2H_5 = R_1CH : CRCOOC_2H_5.$$

If hydrochloric acid or acetic anhydride be used, both aliphatic and aromatic aldehydes can be employed, but if sodium ethoxide or small quantities of diethylamine, piperidine, quinoline, etc., be taken, aromatic aldehydes only will react. In these reactions the methyl gives better results than the ethyl ester.

Esters, such as those of malonic, acetoacetic or cyanoacetic acids, in which the methylene group is doubly activated, will condense even with ketones. By varying the proportion of aldehyde or ketone to ester, 2 mols. of the former can be made to condense with 1 of the latter, using the basic condensing agents only (4, below). The following will illustrate these points :—

(1) $$C_6H_5.CHO + CH_2(COOC_2H_5)_2 \xrightarrow{HCl \text{ or } (CH_3CO)_2O} C_6H_5CH : C(COOC_2H_5)_2.$$
Benzylidenemalonic Ester.

(2) $$CH_3.CHO + RNH_2 \rightarrow CH_3CH : NR + H_2O.$$
$$CH_3CH : NR + CH_2(COOC_2H_5)_2 \rightarrow CH_3CH : C(COOC_2H_5)_2 + NH_2R.$$
Ethylidenemalonic Ester.

(3) $$(CH_3)_2 : CO + CH_3.CO.CH_2.COOC_2H_5 \xrightarrow{C_9H_7N} (CH_3)_2C : C(COCH_3)COOC_2H_5.$$
Isopropylideneacetoacetic Ester.

(4) $$(CH_3)_2CO + 2CN.CH_2.COO.C_2H_5 \rightarrow (CH_3)_2 : C\left\langle\begin{array}{l} CH(CN)COOC_2H_5 \\ CH(CH)COOC_2H_5 \end{array}\right.$$

Preparation 71.—**Ethyl Cinnamate** [*Ethyl ester of 3-phenyl-2-propen acid*].

$$C_6H_5CH : CH.COOC_2H_5. \qquad C_{11}H_{12}O_2. \qquad 176.$$

To 50 gms. (excess) of pure ethyl acetate (see Preparation 199) are added 23 gms. (excess) of sodium in the form of wire. The flask is cooled in ice, and, with slight shaking, 10 gms. (1 mol.) of benzaldehyde are gradually added. When all the sodium has gone into solution, the flask is set aside for 2 hours, when it is acidified with dilute acetic acid. The ester layer which separates is removed, shaken up with dilute sodium carbonate solution, and dried over calcium chloride. It is then distilled, the fraction 265°—275° being retained.

$$C_6H_5CHO + CH_3COOC_2H_5 \xrightarrow{C_2H_5ONa} C_6H_5CH : CH.COOC_2H_5.$$

*Yield.*—65% theoretical (11 gms.). Colourless liquid; insoluble in water; B.P. 271°. (B., 23, 976; O. S., IX., 38.)

This method of preparation can be applied generally to the esters of the phenyl-olefinic acids. Although metallic sodium is used, yet as in the acetoacetic ester synthesis (see Reaction XLVI.) a trace of alcohol must always be present to form sodium ethoxide. This is usually the case. If necessary, sodium ethoxide itself can be employed. The use of some other condensing agents will be clear from the following preparation.

Preparation 72.—**Diethyl Benzylidenemalonate.**

$$C_6H_5CH : C(COOC_2H_5)_2. \qquad C_{14}H_{16}O_4. \qquad 248.$$

8 gms. (1 mol.) of pure dry malonic ester, and 5 gms. (1 mol.) of dry, freshly distilled benzaldehyde are mixed. They can be condensed

with hydrochloric acid gas or ammonia, according to the following methods :—

(i.) *Hydrogen Chloride.*—The mixture is cooled to $-10°$ (see p. 12) and saturated with *dry* hydrogen chloride, the temperature being kept below $-5°$. The whole is then allowed to stand at room temperature for 8 days, and the product worked up as described below.

(ii.) *Ammonia.*—The mixture is allowed to stand with 2 gms. of ammonia in alcoholic solution, until all the benzaldehyde has disappeared.

The product in each case is washed with much water, with dilute hydrochloric acid (especially in (ii.) ) and again with water. It is then dried over anhydrous sodium sulphate and distilled under reduced pressure, the fraction 185°—195° at 12 mms. being retained.

Hydrochloric acid acts directly as a condensing agent. With ammonia the reaction may be formulated—

$$C_6H_5CHO + NH_3 \rightarrow C_6H_5CH : NH + H_2O.$$
$$C_6H_5CH : NH + CH_2(COOC_2H_5)_2 \rightarrow C_6H_5CH : C(COOC_2H_5)_2 + NH_3.$$

Colourless oil ; insoluble in water ; B.P. $^{13}$ 198°. (A., 268, 156 ; D.R.P., 97734.)

Compare this preparation with that of benzylidenemalonic acid (Preparation 53).

PREPARATION 73.—**Tetraethyl Methylenedimalonate.**

$$CH_2[CH(COOC_2H_5)_2]_2. \qquad C_{15}H_{24}O_8. \qquad 332.$$

32 gms. of ethyl malonate and 8 gms. of formalin (40%) are placed in a flask, cooled by immersion in ice, and 0·5 gm. of diethylamine added. The flask is then cooled and left to stand for 12 hours at room temperature, after which it is heated on a boiling water bath for 5—6 hours. The aqueous layer is separated, and the residue distilled under reduced pressure (about 12 mms.). The distillation is conducted slowly, so that all the water passes over below 50°. Methylenedimalonic ester passes over at 190°—200°.

$$CH_2O + 2HN(C_2H_5)_2 \rightarrow CH_2[N(C_2H_5)_2]_2 + H_2O.$$
$$CH_2[N(C_2H_5)_2]_2 + 2CH_2(COOC_2H_5)_2 \rightarrow CH_2\begin{cases} CH(COOC_2H_5)_2 \\ CH(COOC_2H_5)_2 \end{cases} + 2HN(C_2H_5)_2.$$

*Yield.*—80% theoretical (27 gms.). Colourless oil ; insoluble in water ; B.P. $^{18}$, 205° ; B.P. $^{12}$, 198°. (B., 22, 3294 ; 31, 738, 2585, O. S., X., 58.)

PREPARATION 74.—**Diethyl Ethylidenebisacetoacetate** [4-*Methyl*-3 : 5-*carbethoxyl-heptan*-2 : 6-*dione*].

$$\begin{array}{l} CH_3.CO.CH.CH(CH_3)CH.(COOC_2H_5)CO.CH_3 \\ \quad\quad\quad\;\; | \\ \quad\quad\quad COOC_2H_5. \qquad C_{14}H_{22}O_6. \qquad 286. \end{array}$$

8·5 gms. (1 mol.) of *pure freshly distilled* acetaldehyde are slowly added to 50 gms. (2 mols.) of *pure vacuum distilled* cooled acetoacetic ester contained in a thick-walled flask closed by a cork and having a thermometer reaching almost to the bottom. The flask is cooled to $-10°$ to $-15°$ in a freezing mixture of ice and salt. A few drops of diethylamine are then

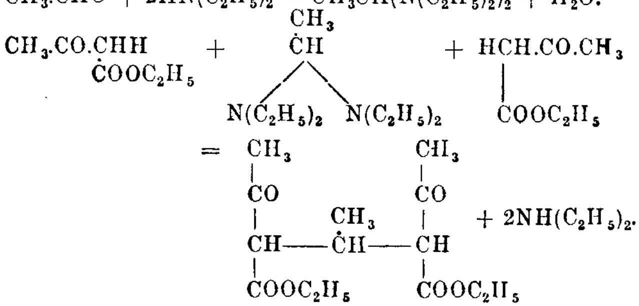
added by means of a burette. Owing to neutralisation of the first portions of the amine by traces of acids nearly always present as impurities, an increase in the temperature seldom takes place at first. After the addition of about 5 drops an elevation of a few degrees will be noticed, and the liquid becomes turbid. From this point a further 5 drops are added slowly, and the temperature is allowed to rise gradually to 0°. 20 more drops are then slowly added with frequent shaking; the whole operation should take about 1 hour. In all, 30 drops (= 1·5 gms.) of the base are required.

The whole is allowed to stand in the freezing mixture for 15 minutes, then removed and allowed to come to room temperature. Should the temperature go up to 20° on account of secondary reactions, the flask is cooled for a short time in ice-water.

The reaction product is a viscous bright yellow liquid in which numerous drops of water are suspended. It is allowed to remain until it solidifies to a crystalline mass; this generally requires from 2—3 days.

If the pure product is required, the mass is pressed on a porous plate and recrystallised from dilute alcohol. The crude product will serve for the preparation of dimethylcyclohexanone (see p. 82). The solidification of the crude product may be hastened by seeding it, after one day's standing, with crystals obtained in a previous preparation. This is best done on the upper portion of the flask, which is only moistened by the liquid.

$$CH_3.CHO + 2HN(C_2H_5)_2 = CH_3CH(N(C_2H_5)_2)_2 + H_2O.$$



*Yield.*—70% theoretical (40 gms.). Colourless needles; M.P. 79°—80°. (A., 323, 83; 332, 1; B., 36, 2118.)

Acetaldehyde and acetoacetic ester in presence of acetic anhydride, hydrochloric acid, ammonia, diethylamine, piperidine, etc., can also be made to yield ethylidene monoacetoacetic ester. (A., 218, 172; B., 29, 172; 31, 735.)

With regard to the intermediate compounds of the types RCH : NR and RCH : $(NRR_1)_2$ postulated in some of the above reactions, it is to be noted that the compounds of the type RCH(OH)NHR and $RCH(OH)NRR_1$ can also be regarded as intermediates.

**Reaction XLVI. Condensation of an Ester with itself or with another Ester by means of Sodium Ethoxide, or Sodamide** (Claisen). (J., (1868), 323; Phil. Mag., 156, 37; A., 186, 161, 214; 201, 243; 213, 137.)—

When sodium ethoxide or sodamide acts on acetic or propionic ester, 2 mols. of the ester condense to yield acetoacetic or propiopropionic ester respectively. In the reaction 1 mol. of alcohol is split off from 2 mols. of ester, the ethoxyl group coming from one molecule, and the hydrogen atom from the α-carbon of a second.

$$\mathrm{CH_3CH_2.COO.C_2H_5} + \begin{array}{c}\mathrm{CH_3}\\ |\\ \mathrm{HCH.COOC_2H_5}\end{array} \xrightarrow{\mathrm{C_2H_5ONa}}$$
$$\mathrm{CH_3CH_2CO.CH(CH_3)COOC_2H_5 + C_2H_5OH.}$$

The reaction can also be extended to condensations between two different esters, it being only necessary that one of the esters should have two α-hydrogen atoms, one to react and one to enable a sodio-derivative to be formed. β-Ketonic compounds always result—this condensation in fact belonging to the same class as those described in Reaction XXIII. (*b*). The higher esters do not condense in the same manner. When sodium acts on normal butyric ester, *iso*-butyric ester, *iso*-valeric ester, etc., the resulting compounds are not analogous, being hydroxy-alkyl derivatives of higher fatty acids (A., 249, 54). Some di-basic esters in undergoing the condensation yield ring compounds; this is an especially important feature of the reactions (see p. 147).

The mechanism of the process must be now considered. The reaction between metallic sodium and ester occurs in the presence of a trace of alcohol (B., 3, 305), so sodium ethoxide must be regarded as the condensing agent (*cf.* Reaction XLV., p. 142). This view is supported by the fact that separately prepared sodium ethoxide gives almost as good a yield as metallic sodium. See also J. A. C. S., 53, 2310.

The first step in the synthesis may be taken to be—

$$\mathrm{CH_3CO.OC_2H_5 + C_2H_5ONa \longrightarrow} \underset{\mathrm{I.}}{\mathrm{CH_3C}\!\begin{array}{l}\diagup\mathrm{OC_2H_5}\\ -\mathrm{ONa}\\ \diagdown\mathrm{OC_2H_5}\end{array}} \quad \text{or} \quad \underset{\mathrm{II.}}{\begin{array}{l}\mathrm{CH_2}\\ \|\\ \mathrm{C.OC_2H_5}\\ \mathrm{ONa}\end{array}}$$

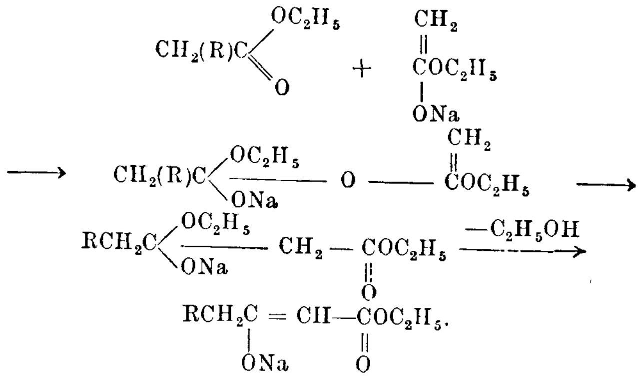
II. results from I. by the loss of alcohol, but I. is more probably the intermediate compound, because methyl benzoate and sodium benzoxide give the same compound—actually isolated—as benzyl benzoate and sodium methoxide.

$$\begin{array}{l}\mathrm{C_6H_5COOCH_3 + C_6H_5CH_2ONa} \longrightarrow \\ \mathrm{C_6H_5COOCH_2C_6H_5 + CH_3ONa} \nearrow\end{array} \mathrm{C_6H_5C}\!\begin{array}{l}\diagup\mathrm{ONa}\\ -\mathrm{OCH_3}\\ \diagdown\mathrm{OCH_2C_6H_5}.\end{array}$$

I. then reacts with the still unchanged ester or with a molecule of the other ester—

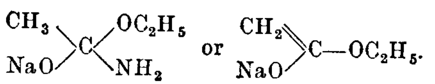
$$\begin{array}{l}\mathrm{CH_3}\diagdown\\ \mathrm{NaO}\diagup\end{array}\!\mathrm{C}\!\begin{array}{l}\diagup\mathrm{OC_2H_5}\\ \diagdown\mathrm{OC_2H_5}\end{array} + \begin{array}{l}\mathrm{H}\diagdown\\ \mathrm{H}\diagup\end{array}\!\mathrm{C(R)COOC_2H_5} \longrightarrow$$
$$\begin{array}{l}\mathrm{CH_3C : C(R)COOC_2H_5 + 2C_2H_5OH.}\\ \quad\;|\\ \;\;\mathrm{ONa}\end{array}$$

or else a molecule of ester and a molecule of II. unite and then split off alcohol, with rearrangement.



(A., 297, 92 ; B., 36, 3678 ; 38, 714, 1934.) Both assumptions coincide equally well with the fact that fatty acid esters do not condense analogously to the above, with secondary and tertiary alkyl groups.

Sodamide can also be employed as condensing agent. The intermediate compound is then—

I.  II.

It is in favour of II. that it is an intermediate compound independent of the condensing agent. For the influence of solvents on the reaction, see C., (1907), II., 30.

The following examples are of interest :—

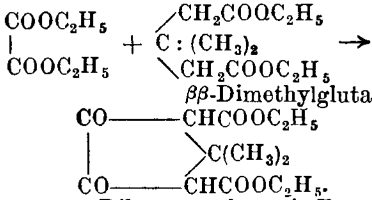
(i.) $$H.COOC_2H_5 + CH_3.COOC_2H_5 \xrightarrow{C_2H_5ONa} H.CO.CH_2COOC_2H_5 + C_2H_5OH.$$

Formylacetic Ester.
(Hydroxymethyleneacetic Ester).

The above reaction goes best in ethereal or benzene solution.

(ii.) $$\begin{array}{l}COOC_2H_5\\ |\\ COOC_2H_5\end{array} + CH_3.COOC_2H_5 \rightarrow C_2H_5O.CO.CO.CH_2.COOC_2H_5. + C_2H_5OH.$$

Oxalacetic Ester

(iii.) 

ββ-Dimethylglutaric-diethylester.

Diketocamphopyric Ester.

This is an important step in the synthesis of camphor (see Reactions XLIV. (*b*) (3) ).

Attention is directed to the discussion of other theories bearing on the mechanism of reactions in which metallic alkyl-oxides play a prominent part.

See Ann. Rep., 1934, 193.

PREPARATION 75.—**Ethyl Acetoacetate** [*Ethyl ester of* 3-*on-butan acid*].

$CH_3COCH_2COOC_2H_5$ and $CH_3C(OH):CH.COOC_2H_5$. $C_6H_{10}O_3$. 130.

250 gms. of commercial ethyl acetate are shaken with sodium carbonate solution, separated and allowed to stand for 24 hours over freshly fused calcium chloride, filtered into a distilling flask, and redistilled, care being taken that all parts of the apparatus are dry.

20 gms. (1 atom) of sodium in the form of wire are placed in a clean dry ½-litre round-bottomed flask. The latter is attached to a long reflux condenser, and 200 gms. (excess) of the purified ethyl acetate are slowly introduced through the top of the condenser. When the first action is over, the whole is heated on a water bath to gentle ebullition for 3 hours, when 150 gms. of 50% acetic acid are added gradually till the mixture is just acid (test with litmus). The whole is well shaken to redissolve any deposited solid, and the mixed ethyl acetate and ethyl acetoacetate separated by adding an equal volume of saturated brine. Should a precipitate separate a little water is added to dissolve it. The upper layer of the mixed esters is fractionally distilled under reduced pressure, the fraction 85°—95° at 40 mms. separately collected and redistilled under reduced pressure. The residue in the flask contains dehydracetic acid (see Preparation 65). To obtain the best results the experiment must be completed in one day.

$$CH_3.C\begin{cases}OC_2H_5\\OC_2H_5\\ONa\end{cases} + CH_3.COOC_2H_5 = \begin{array}{c}CH_3.C:CHCOOC_2H_5\\ \dot{O}\\ \dot{N}a\end{array}$$

$$\begin{array}{l}CH_3.C:CHCOOC_2H_5\\ \quad|\\ \quad ONa\end{array} + CH_3.COOH = \begin{array}{l}CH_3.C:CHCOOC_2H_5\\ \quad\dot{O}H\end{array}$$

$$\begin{array}{l}CH_3.C:CHCOOC_2H_5\\ \quad\dot{O}H\end{array} \rightleftarrows CH_3.CO.CH_2.COOC_2H_5.$$

*Yield.*—20% theoretical (44 gms.). Colourless liquid ; slightly soluble in water ; B.P. $^{760}$ 181° ; B.P. $^{12}$ 72° ; D. $^{20}_{4}$ 1·0256 (O. S., VI., 36).

The following methods have been used for the separation of the keto and enol forms of ethyl acetoacetate.

The ester is first fractionally distilled at 10 mm. in glass apparatus, thus becoming highly enolised (80—90%), and then immediately fractionated in quartz, the first fraction being pure enol. (B., 53, 1410 ; 54, 579.)

By cooling a concentrated solution of the ester in different solvents to — 78°, the pure keto (M.P.—39°) separates, which gives no coloration with ferric chloride. The enol form is obtained by treating the sodium salt

with dry hydrogen chloride at − 78°. (B., 44, 1147.) Both compounds form the same equilibrium mixture at ordinary temperature.

For the estimation of the amount of keto and enol forms present in the equilibrium mixture, see p. 496.

**Reaction XLVII. Condensation of an Ester with itself by the action of Iodine on its Sodio-derivative.** (B., 23, R., 141; A., 201, 144; 266, 88.) When iodine, usually in ethereal solution, acts on the sodio-derivatives of esters, such as malonic or acetoacetic esters, the metal is eliminated, and higher dibasic esters are obtained. As will be seen, the reaction is especially useful for preparing cyclo-paraffins by acting with iodine (or bromine) upon disodio-methylene- and disodio-ethylene-, etc., di-malonic esters.

(*a*)

$$\begin{array}{l} COOC_2H_5 \\ | \\ HC \\ \| \\ C.ONa \\ | \\ OC_2H_5 \end{array} + I_2 + \begin{array}{l} COOC_2H_5 \\ | \\ HC \\ \| \\ C.ONa \\ | \\ OC_2H_5 \end{array} \rightarrow$$

$$(C_2H_5OOC)_2\overset{H}{C}—\overset{H}{C}(COOC_2H_5)_2$$

Ethanetetracarboxylic Ester
(Dimalonic Ester.)

(*b*)

$$CH_2\begin{cases} CNa(COOC_2H_5)_2 \\ CNa(COOC_2H_5)_2 \end{cases} + I_2 \rightarrow CH_2\begin{cases} C(COOC_2H_5)_2 \\ | \\ C(COOC_2H_5)_2. \end{cases}$$

Disodio-methylenedimalonic Ester (Propanetetracarboxylic Ester.) — *Cyclo*propanetetracarboxylic Ester.

(*c*)

$$CH_2\begin{cases} CH_2CNa(COOC_2H_5)_2 \\ CH_2CNa(COOC_2H_5)_2 \end{cases} + I_2 \longrightarrow$$

Disodio-propylenedimalonic Ester
(Pentanetetracarboxylic Ester.)

$$CH_2\begin{cases} CH_2.C(COOC_2H_5)_2 \\ \qquad | \\ CH_2.C(COOC_2H_5)_2. \end{cases}$$

*Cyclo*pentanetetracarboxylic Ester.

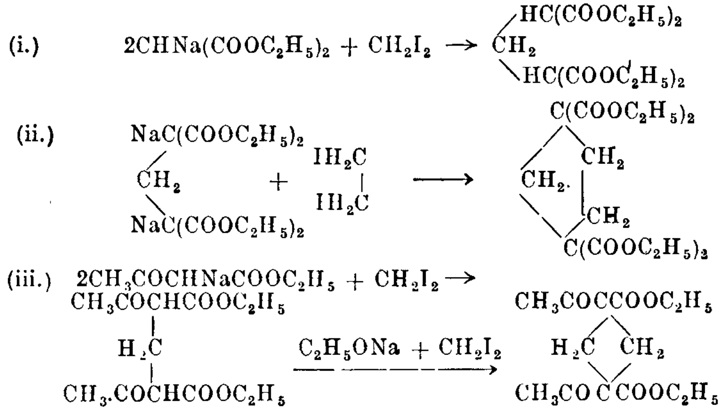
*Cf.* Reaction XLIV. (*a*) (iii.).

(*d*)

$$2CH_3.CO.CHNaCOOC_2H_5 + I_2 \rightarrow \begin{array}{l} CH_3\,CO\,CHCOOC_2H_5 \\ \qquad\quad | \\ CH_3.CO.CH.COOC_2H_5. \end{array}$$

Diacetosuccinic Ester.

The action of methylene and ethylene iodides, etc., on the sodio-derivatives of the esters dealt with above might have been discussed under Reaction XLIV. (*a*), but is best dealt with here. The di-iodides react analogously to the iodine molecule; extra carbon is of course introduced into the reacting molecules. The following illustrates :—



It will be seen that whereas iodine leads to 1 : 2 tetra- and di-basic esters, methylene, ethylene, etc., iodides yield respectively 1 : 3, 1 : 4, etc., esters. The yields in these ring syntheses, as in most others, vary in agreement with Baeyer's "Strain Theory."

PREPARATION 76.—**Diethyl Diacetosuccinate** (*αβ-Dicarbethoxy-αβ-diacetoethane*).

$$\begin{array}{ll} CH_3.COCH\text{—} & CH.CO.CH_3. \\ \quad\quad\quad\ | & \ | \\ C_2H_5OOC & COOC_2H_5. \end{array} \qquad C_{12}H_{18}O_6. \qquad 258.$$

In a stoppered bottle of 500 c.cs. capacity provided with a reflux condenser, 25 gms. (2 mols.) of acetoacetic ester are dissolved in 150 gms. of pure ether which has been dried over sodium, and to this solution 5 gms. (2 mols.) of fine sodium wire are added. After 2 hours, the bottle is shaken at intervals, being stoppered while so doing, till no further evolution of hydrogen takes place, and all the metal has been converted into sodio-acetoacetic ester. 20 gms. (excess) of finely powdered iodine are dissolved in pure anhydrous ether, and the solution added in small portions, and with constant shaking, to the solution of the sodio-acetoacetic ester. Sodium iodide is precipitated as soon as the colour of the iodine no longer vanishes at once, the solution is filtered, the ether evaporated off, and the diacetosuccinic ester allowed to solidify. It is then pressed on a porous tile, and recrystallised from warm 50% acetic acid.

$$2CH_3CO.CH_2COOC_2H_5 \xrightarrow{2Na} 2CH_3C(ONa):CHCOOC_2H_5 \xrightarrow{I_2}$$

$$\begin{array}{ll} CH_3.CO.CH\ \text{—} & CH.CO.CH_3 \\ \quad\quad\quad\quad | & | \\ C_2H_5OOC & COOC_2H_5. \end{array}$$

*Yield.*—40% theoretical (10 gms.). Colourless crystals; plates when crystallised slowly; needles when crystallised rapidly; soluble in ether; insoluble in water; M.P. 88°. (B., 7, 892; A., 266, 88.)

(*Cf.* Reaction XXXVII.)

# CHAPTER VIII

## CARBON TO CARBON

### NITROGEN COMPOUNDS

NITROGEN enters into the constitution of many carbon compounds, and such nitrogen-containing compounds are usually very reactive; in addition to reacting with other compounds a great number readily undergo intramolecular transformations. Nitrogen also plays an important part in ring formation; nitrogen-containing rings are very stable, and the condensations which give rise to them many and various. On this account a great many important reactions and preparations come to be dealt with in this section; of these, however, only a small selection can be given.

**Reaction XLVIII.** (*a*) **Action of Alkali Cyanides on Alkyl and Acyl Halides.** (Bl., [2], 50, 214.)—This reaction is capable of very wide application, all the simple alkyl halogen compounds, the acyl halides, and the halogen fatty acids come within its scope. The nitriles so formed yield acids by hydrolysis, so it is frequently the first step in the synthesis of an acid—the preparation and hydrolysis of the nitrile are often combined. The preparations of malonic, succinic, tricarballylic and other acids (Preparations 60, 61, 62) illustrate this. The extension of this reaction to acyl halides is important, and should be referred to, as should the interaction of silver cyanide, and alkyl iodides, to give isonitriles. Mercuric and silver cyanides, it may be noted, give with acyl chlorides and bromides better yields of normal acyl nitriles than do the alkali cyanides.

In reactions where nitriles are prepared from halogen compounds by double decomposition with alkali cyanide in alcoholic or aqueous alcoholic solution, the latter is usually added in solution or as a powder (*cf.* Preparations 77, 78, 79), otherwise the alkali halide which separates forms a coating round the cyanide and hinders further action. If the reaction is performed in aqueous solution, as in the preparation of malonic acid (p. 125), this precaution is not so necessary; the alkali halide, when formed, remains in solution.

PREPARATION 77.—**Succinonitrile** (*Ethylene Cyanide*).

$$\begin{array}{l} CH_2.CN \\ | \\ CH_2.CN. \end{array} \qquad C_4H_4N_2. \qquad 80.$$

The solution of the nitrile prepared as in Preparation 61 from 100 gms. (1 mol.) of ethylene dibromide and 75 gms. (excess) of potassium cyanide, after filtration from the separated potassium bromide, is evaporated on a

water bath under reduced pressure. The residue is extracted with absolute alcohol, the extract evaporated as before, and the residue fractionated under reduced pressure, the fraction 144°—150° at 10 mms. being retained.

$$\begin{array}{l} CH_2Br \\ | \\ CH_2Br \end{array} + 2KCN = \begin{array}{l} CH_2CN \\ | \\ CH_2CN \end{array} + 2KBr.$$

*Yield.*—80% theoretical (34 gms.). Amorphous transparent mass; readily soluble in water, chloroform and alcohol; sparingly soluble in ether; M.P. 54·5°; B.P., $^{10}$ 147°; B.P. $^{20}$ 159°. (Bl., [2], 50, 214.)

Propenyl tricyanide, the nitrile of tricarballylic acid, is obtained in a similar manner (see Preparation 62).

PREPARATION 78.—**Phenylacetonitrile** (*Benzyl Cyanide*).

$$C_6H_5.CH_2.CN. \qquad C_8H_7N. \qquad 117.$$

60 gms. (slightly more than 1 mol.) of commercial potassium cyanide are dissolved in 55 gms. of water in a $\frac{3}{4}$-litre round-bottomed flask fitted with a reflux condenser and placed in a fume cupboard. 100 gms. (1 mol.) of benzyl chloride dissolved in 100 gms. of alcohol are poured slowly into the hot solution of potassium cyanide through the top of the condenser, and the whole gently boiled for 4 hours on a sand bath. The flask is then cooled, and the upper dark brown liquid, consisting of an alcoholic solution of benzyl cyanide, is decanted from the crystalline deposit of potassium chloride and distilled over wire gauze in a fume cupboard, the fraction 210°—235° being retained. It is crude benzyl cyanide, and can be used for Preparation 176.

To prepare the pure substance, this fraction is redistilled and collected at 230°—235°.

$$C_6H_5CH_2Cl + KCN = C_6H_5CH_2CN + KCl.$$

*Yield.*—80% theoretical (75 gms.). Colourless, pungent smelling liquid; B.P., 232°; D. $^{17·5}_{4}$ 1·0171. (A., 96, 247; B., 14, 1645; 19, 951; O. S., II., 9).

**Reaction XLVIII.** (*b*) **Action of Alkali Cyanides on Alkyl Hydrogen Sulphates.** (A., 10, 249.)—The alkyl nitriles may also be prepared by dry distilling alkali cyanides with alkali-alkyl-sulphates.

$$M_1CN + SO_2(OM_{11})OR = RCN + SO_2(OM_{11})(OM_1).$$

PREPARATION 79.—**Propionitrile** (*Ethyl Cyanide*).

$$C_2H_5CN. \qquad C_3H_5N. \qquad 55.$$

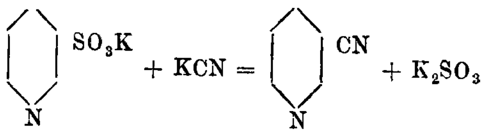
50 gms. (excess) of *finely powdered* (*caution!*), dry, commercial potassium cyanide and 50 gms. (1 mol.) of *finely powdered* potassium ethyl sulphate dried at 100° are intimately mixed. An iron tube, closed at one end, is one-third filled with the mixture. The tube is tapped while in a horizontal position to form a channel along the upper surface of the mixture, is placed in a combustion furnace so that the open end projects 3 cms. from the furnace, and connected with a condenser and receiver, all being set up in a fume cupboard. The mixture is then gradually heated,

from the front backwards, to a red heat. The distillate is redistilled to 110°, and the second distillate (propionitrile, isopropionitrile, alcohol and water) shaken with a small quantity of conc. hydrochloric acid to remove isopropionitrile, washed with a small quantity of water, dehydrated over calcium chloride or anhydrous potassium carbonate and fractionated between 97° and 101°. The propionitrile dissolved in the washings is separated by adding calcium chloride, and worked up as above.

$$C_2H_5.O.SO_2.OK + KCN = KO.SO_2.OK + C_2H_5CN.$$

*Yield.*—60% theoretical (10 gms.). Colourless liquid, peculiar ethereal smell; slightly soluble in water; B.P. 98°; D. $^{12}_{4}$ 0·789. (A., 10, 249; 148, 252; 159, 79.)

A somewhat similar method of cyanide preparation is applicable in the aromatic series; aromatic sulphonic acid potassium salts, on fusion with potassium cyanide or potassium ferrocyanide, yield aromatic nitriles. The reaction can be extended to derivatives of pyridine.




(Nicotinonitrile.)

**Reaction XLVIII.** (*c*) **Action of Dimethyl Sulphate on Potassium Cyanide.** (B., 40, 3215.)—This method gives excellent yields of acetonitrile; diethyl sulphate yields propionitrile by a similar method.

PREPARATION 80.—**Acetonitrile** (*Methyl Cyanide*).

$$CH_3CN. \quad C_2H_3N. \quad 41.$$

68 gms. (1 mol.) of finely powdered potassium cyanide are dissolved in 60 c.cs. of water, in a 500-c.c. round-bottomed flask, and after cooling 126 gms. (1 mol.) of dimethyl sulphate (*caution!* see p. 261) are added in three equal portions, the whole being shaken vigorously and cooled under water after each addition. During the shaking, the flask is closed by a one-holed cork carrying a glass tube bent three or four times, so as to form a spiral, having its axis horizontal. This prevents spurting out of any liquid. The milky liquid is distilled on a water bath in a fume cupboard at 82°, a litre flask being used owing to frothing. The residue in the flask is treated on cooling with another 65 gms. (1 mol.) of potassium cyanide, added slowly, in 50% solution as before, and the whole is very cautiously distilled from a water bath. A violent reaction occurs, and when this has slackened, the distillation is continued until the residue in the flask becomes solid and nothing more comes over. The distillate is removed and shaken with half its volume of water; solid potassium carbonate is added until no more dissolves, the layer of nitrile is separated from the aqueous solution and redistilled over phosphorus pentoxide, the fraction 79°—83° being retained.

$$KCN + (CH_3)_2SO_4 = (CH_3)KSO_4 + CH_3CN.$$
$$CH_3KSO_4 + KCN = K_2SO_4 + CH_3CN.$$

*Yield.*—95% theoretical (78 gms.). Colourless liquid; ethereal odour; slightly soluble in water; B.P. 82°. (B., 40, 3215.)

**Reaction XLIX.** (*a*) **Action of Cuprous Potassium Cyanide on Aromatic Diazonium Compounds.** (Sandmeyer). (B., 17, 1633, 2650; 18, 1492, 1496.)—If a diazonium salt is added to a hot solution of cuprous-potassium cyanide, and the whole boiled on a water bath, nitrogen is evolved, and the corresponding nitrile formed. (C. r., 183, 421.)

$$2R.N_2Cl + KCN(CuCN)_2 \longrightarrow 2RCN + 2N_2 + KCN + Cu_2Cl_2.$$

As usual in Sandmeyer reactions, the product, if volatile, is separated by distillation in steam; if non-volatile, extraction or filtration is used. The manner in which the cuprous salt reacts is not exactly known; it certainly unites at first with the diazonium compound to form a double salt (*cf.* Reaction CLXVI.). The method is widely applicable, and as the yields are usually good, it is a standard method for the preparation of aromatic nitriles.

Preparation 81.—**Benzonitrile** (*Phenyl Cyanide*).

$$C_6H_5.CN. \qquad C_7H_5N. \qquad 103.$$

The details of this preparation are practically the same as those given for *p*-tolu-nitrile (Preparation 82). A cuprous-potassium cyanide solution, prepared as therein described, is warmed to about 70°, and added in small portions to a solution of benzene-diazonium chloride prepared from 18·6 gms. (1 mol.) of aniline as described in Preparation 379. When the addition is complete, the liquid is warmed on a water bath for 15 minutes and distilled in steam; the distillate is extracted with ether. The ethereal solution is washed repeatedly with dilute caustic soda and with dilute sulphuric acid, dried over anhydrous potassium carbonate, filtered, and the oil which remains on driving off the ether fractionated. Owing to the evolution of cyanogen and hydrocyanic acid, this preparation *must* be carried out in a *good* fume cupboard.

$$C_6H_5NH_2 \xrightarrow[HCl]{HNO_2} C_6H_5.N_2.Cl \xrightarrow{Cu_2CN_2.KCN} C_6H_5CN.$$

*Yield.*—65% theoretical (13 gms.). Colourless oil; odour resembling that of benzaldehyde or nitrobenzene; insoluble in water; soluble in ether; B.P. 191°. (B., 17, 2653. See also O. S., IV., 69.)

Preparation 82.—***p*-Toluonitrile** (1-*Methyl*-4-*cyanobenzene*).

$$CH_3.C_6H_4.CN.[1.4]. \qquad C_8H_7N. \qquad 117.$$

50 gms. (1 mol.) of copper sulphate crystals are dissolved in 200 c.cs. of water, and 56 gms. (excess) of 96% potassium cyanide added to the warm solution. As cyanogen is evolved, the operation must be carried out in a good fume cupboard, and the fumes must on no account be inhaled, 20 gms. (1 mol.) of *p*-toluidine are then diazotised as in Preparation 397, and the diazo solution gradually added in a $\frac{1}{4}$ hour, from a dropping funnel to the cuprous-potassium cyanide solution at 90°, the mixture being kept well shaken. The product is heated on a water bath for a $\frac{1}{4}$ hour, and

distilled in steam in a good fume cupboard, since hydrogen cyanide and a little isocyanide are formed; the solid distillate is filtered off, dried on a porous plate, and redistilled.

$$CuSO_4 + 2KCN = Cu(CN)_2 + K_2SO_4.$$
$$2Cu(CN)_2 = Cu_2(CN)_2 + (CN)_2.$$
$$Cu_2(CN)_2 + KCN = 2CuCN.KCN.$$
$$2CH_3.C_6H_4N_2Cl + 2CuCN.KCN = 2CH_3.C_6H_4.CN + 2N_2 + Cu_2Cl_2 + KCN.$$

*Yield.*—65% theoretical (14 gms.). Colourless crystals; insoluble in water; soluble in ether; M.P. 24°; B.P. 218°. (B., 17, 2653.)

*o*-Toluonitrile is prepared in an exactly similar fashion from *o*-toluidine. It boils at 205°; D. $^0_4$ 1·006. (O. S., IV., 69.)

**Reaction XLIX.** (*b*) **Action of finely divided Copper and Alkali Cyanides on Aromatic Diazonium Compounds** (Gattermann). (B., 23, 1218.)—This is the Gattermann modification of the preceding Sandmeyer reaction; as usual, the cuprous salt is replaced by finely divided copper. This method gives better yields of some aromatic nitriles.

PREPARATION 83.—**Benzonitrile** (*Cyanobenzene*).

$$C_6H_5CN. \qquad C_7H_5N. \qquad 103.$$

(*This reaction must be carried out in a good fume cupboard.*)

31 gms. (1 mol.) of aniline are dissolved in 80 gms. (excess) of 50% sulphuric acid, the solution cooled to 0° by addition of ice, and the base diazotised by the addition of 23 gms. (1 mol.) of sodium nitrite as described in Preparation 379. 80 gms. (excess) of 96% potassium cyanide in 50% solution are poured in, and then, with constant stirring, 40 gms. of copper paste (see p. 508) are added in small quantities, and the whole allowed to stand until the evolution of nitrogen ceases and the copper sinks to the bottom of the vessel. The reaction is then over. The product is steam distilled, and the nitrile extracted and purified as described under Preparation 81.

$$C_6H_5N_2SO_4H + KCN(Cu) = C_6H_5CN + KHSO_4 + N_2(Cu).$$

*Yield.*—60% theoretical (20 gms.). Colourless oil; insoluble in water; soluble in ether; odour resembling that of benzaldehyde or nitrobenzene; B.P. 191°. (B., 23, 1218.)

The preparation of *o*- or *p*-toluonitrile is exactly similar.

**Reaction L.** (*a*) **Addition of Hydrogen Cyanide to Aldehydes or Ketones.** (B., 14, 235; 39, 1224, 1857; 28, 10; C. Z., (1896), 90.)—Hydrocyanic acid combines with aldehydes and ketones to yield α-hydroxynitriles (cyanohydrins).

$$RR_1CO + HCN \longrightarrow RR_1C(OH)CN.$$

Nascent hydrogen cyanide formed by the action of hydrochloric acid on potassium cyanide is usually employed except with sugars, where hydrocyanic acid and a little ammonia are used. The manner in which ammonia promotes the action, and the better results obtained by the use of the bisulphite compound of the aldehydes and potassium cyanide, have been dealt with under Reaction XXXVIII. (*c*).

Preparation 64 illustrates the importance of this reaction in the sugar group. For the hydrolysis of nitriles, see p. 239.

PREPARATION 84.—**Acetone Cyanohydrin** (*β-Hydroxy-β-cyanopropane*).

$(CH_3)_2C(OH)CN$. $C_4H_7ON$. 85.

10 gms. (1 mol.) of acetone are shaken with a saturated sodium bisulphite solution containing 18 gms. (1 mol.) of $NaHSO_3$, and, after cooling, 30 gms. (excess) of a cold 50% solution of 96% potassium cyanide are slowly added. The crystalline bisulphite compound soon dissolves and a fluorescent oil is formed. This is extracted several times with ether, and the ethereal extracts are shaken with saturated bisulphite solution (to remove acetone) and then washed with saturated brine. The ether is removed on a water bath, and the residual oil dried under reduced pressure over conc. sulphuric acid. It is then fractionated under reduced pressure, the fraction 80°—85° at 23 mms. being retained.

$$(CH_3)_2CO + NaHSO_3 = (CH_3)_2C\begin{cases} OH \\ OSO_2Na \end{cases}$$

$$(CH_3)_2C\begin{cases} OH \\ O.SO_2Na \end{cases} + KCN = (CH_3)_2C\begin{cases} OH \\ CN \end{cases} + KNaSO_3.$$

*Yield.*—96% theoretical (15 gms.). Colourless, odourless liquid; soluble in water; soluble in ether; B.P. $^{23}$ 82°. (B., 39, 1225, 1857; Rec., 28, 10; C. Z., (1896), 90; O. S., XI., 4; XV., 1.)

The action of hydrogen cyanide on the aldehyde itself, and the action of potassium cyanide on the bisulphite compound, are directly contrasted in the following preparation.

PREPARATION 85.—**Mandelonitrile** (*Phenylhydroxycyanomethane*).

$C_6H_5CH(OH)CN$. $C_8H_7ON$. 133.

*Method I.*—14 gms. (1 mol.) of finely powdered 96% potassium cyanide, and 20 gms. (1 mol.) of freshly distilled benzaldehyde are placed in a flask cooled with ice and salt. The quantity of the most conc. hydrochloric acid available, corresponding to 7 gms. (1 mol.) of anhydrous acid (about 20 gms. conc. acid will be required), are slowly dropped in with frequent shaking. This must be done in a good fume cupboard. The whole is allowed to stand for 1 hour, being shaken at frequent intervals; it is then poured into 5 volumes of water, and the oil which separates well washed with water several times; a further purification is impossible owing to its instability.

$$C_6H_5.CHO + KCN + HCl = C_6H_5CH(OH)CN + KCl.$$

*Yield.*—Theoretical (26 gms.). (B., 14, 235.)

*Method II.*—50 c.cs. (excess) of a saturated solution of sodium bisulphite are added to 15 gms. (1 mol.) of freshly distilled benzaldehyde in a beaker, and the whole stirred until the mass is semi-solid owing to the separation of the bisulphite compound of the aldehyde. The latter is filtered off at the pump, pressed, and washed with a little water and alcohol. It is then

stirred up with water to a thick paste, and a 30% solution of 12 gms. (excess) of potassium cyanide is added. After stirring for a short time, the crystals go into solution and the nitrile appears as an oil, which is separated and washed with water as above.

$$C_6H_5CHO + NaHSO_3 = C_6H_5CH(OH)O.SO_2Na.$$
$$C_6H_5CH(OH)O.SO_2Na + KCN = C_6H_5CH(OH)CN + KNaSO_3.$$

*Yield.*—Theoretical (20 gms.). M.P. 29°; decomposes on heating. (B., 39, 1224; D.R.P., 85230; C. Z., (1896), 90; B., 64, 427.)

**Reaction L.** (*b*) **Condensation of an Aldehyde with Ammonia and Hydrogen Cyanide** (Strecker-Tiemann-Bucherer-Knoevenagel). A., 75, 27; 94, 234; 176, 341; 211, 359; B., 13, 381; 33, 2372; 39, 989, 1722, 2796, 4059, 4073, 4087.)—When an aldehyde-ammonia is treated with hydrogen cyanide, an amino-nitrile is formed.

$$R.CH(OH)NH_2 + HCN = RCH(CN)NH_2 + H_2O.$$

The two steps in this synthesis are interchangeable (B., 13, 381).

$$R.CH(CN)OH + NH_3 = RCH(CN)NH_2 + H_2O.$$

The use of the conc. hydrocyanic acid necessary in the above reactions can be avoided, and the amino-nitrile synthesised in one stage by using ammonium cyanide or an equimolecular mixture of ammonium chloride and potassium cyanide; this also brings ketones within the scope of the reaction (O. S., XI., 4). The condensation is carried out in aqueous or aqueous alcoholic solutions. An extension of this reaction permits the use of primary aromatic amines and potassium cyanide in place of ammonium chloride and potassium cyanide (D.R.P., 157710; 157709; 158090, 158346; J. C. S., 1931, 653; Am. Soc., 53, 2809.)

Better results are here obtained by using the bisulphite compound of the aldehyde or ketone (*cf.* Reaction L. (*a*)).

$$RR_1CO \longrightarrow RR_1C(OH)SO_3Na \xrightarrow{ArNH_2 + KCN} RR_1C(CN)(NHAr).$$

In the following preparation, the amino-nitrile formed is hydrolysed directly to the corresponding amino-acid. These latter are of great importance in the chemistry of the proteins.

Preparation 86.—**Racemic Leucine** [Racemic-4-*methyl*-2-*amino-pentan acid*].

$$(CH_3)_2.CH.CH_2.CH(NH_2).COOH. \qquad C_6H_{13}O_2N. \qquad 131.$$

(*This preparation must be carried out in a good fume cupboard.*)

50 gms. (1 mol.) of pure redistilled *iso*-valeric-aldehyde are dissolved in 100 c.cs. of absolute ether (see p. 216) and the solution cooled in ice and saturated with dry ammonia (see p. 506). The water formed in the reaction is separated by means of a funnel, the ethereal solution is shaken with a little potassium carbonate, filtered, and evaporated under reduced pressure at a temperature not greater than 25°. The oily residue of *iso*-valeraldehyde-ammonia which usually crystallises rapidly is at once suspended in 100 c.cs. of water; the liquid is cooled, and 36 c.cs. (1 mol.

HCN) of 50% hydrocyanic acid are gradually added (*caution !*). The mixture is allowed to stand, with frequent shaking, for 12 hours, and then a mixture of 400 c.cs. (excess) of conc. hydrochloric acid (D. 1·19) and 200 c.cs. of water is added. This produces a lumpy precipitate, which is dissolved by prolonged boiling in a flask; another 200 c.cs. of water are added, and the boiling continued for 2 hours more. The mixture is finally evaporated to dryness on a water bath to remove hydrochloric acid. The residue is warmed with about 60 c.cs. of water and made faintly alkaline with ammonia. When cold, the leucine which has separated is filtered off at the pump and washed with cold water until all the ammonium chloride has been removed. Further purification is effected by recrystallising from hot water with the addition of animal charcoal. The mother liquor is concentrated or treated with absolute alcohol to obtain any leucine remaining dissolved therein.

$$(CH_3)_2 : CH.CH_2.CHO + HN_3 = (CH_3)_2.CH.CH_2.CH(OH)NH_2$$
$$(CH_3)_2 : CH.CH_2CH(OH)(NH_2) + HCN = (CH_3)_2.CH.CH_2.CH(CN)(NH_2) + H_2O.$$
$$(CH_3)_2 : CH.CH_2.CH(CN)(NH_2) \xrightarrow{H_2O} (CH_3)_2 : CH.CH_2CH.(NH_2)COOH.$$

*Yield.*—33% theoretical (25 gms.). Shining leaflets; slightly soluble in cold water; very slightly in hot alcohol; decomposes on heating. (A., 94, 243; 316, 145; B., 33, 2372.)

PREPARATION 87.—**o-Carboxyphenaminoacetonitrile** (1-(*cyanomethylamino*)-2-*carboxy-benzene*).

$C_6H_4.(NH.CH_2CN)(COOH)[1:2]$. $C_9H_8O_2N_2$. 176.

*Method I.*—7 gms. (1 mol.) of finely powdered potassium cyanide and 14 gms. (1 mol.) of finely powdered anthranilic acid are suspended in 50 c.cs. of ether or benzene in a flask fitted with a reflux condenser. The whole is well cooled in a freezing mixture, and 7·5 c.cs. (1 mol. $CH_2O$) of 40% formalin are slowly added. A brisk reaction sets in, and two layers are formed, the lower of which solidifies on cooling to a mass of crystals of the potassium salt of the required acid. This is collected, dissolved in water, the free acid precipitated by acidification with acetic or hydrochloric acid, washed with cold water, and recrystallised from alcohol, benzene, or chloroform.

$$C_6H_4(NH_2)(COOH)[1:2] \xrightarrow{CH_2O} CH_2(OH).NHC_6H_4.COOH[1:2]$$
$$\xrightarrow{K.CN} CH_2(CN).NH.C_6H_4COOK[1:2] \xrightarrow{HCl} CH_2(CN)NH.C_6H_4COOH[1:2].$$

*Yield.*—Theoretical (18 gms.).

*Method II.*—20 c.cs. (1 mol. $NaHSO_3$) of 40% sodium bisulphite solution, and 7·5 c.cs. (1 mol. $CH_2O$) of 40% formalin are mixed, and the mixture kept at 60°—70° for about 20 minutes until the smell of formaldehyde has vanished. A solution of 14 gms. (1 mol.) of anthranilic acid in 10·3 c.cs. (exactly 1 mol. NaOH) of 30% caustic soda solution is then added and the whole heated on a water bath until no more anthranilic acid is

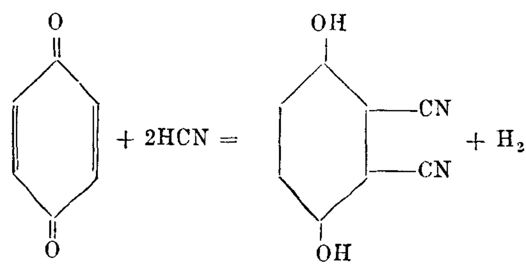
present (about 45 minutes). To test the reaction mixture, a sample is withdrawn at intervals, acidified with an excess of acetic acid, a few drops of sodium nitrite added to the well-cooled mixture, and the whole poured into an alkaline solution of R-salt. Anthranilic acid is absent when no red azo-colour is obtained. When the test is negative, or nearly so, a solution of 7 gms. (1 mol.) of potassium cyanide in 25 c.cs. of water is added, and the whole heated to 70°—80° for 20 minutes. On cooling, an excess of glacial acetic acid is added, and the nitrile filtered off and purified as before.

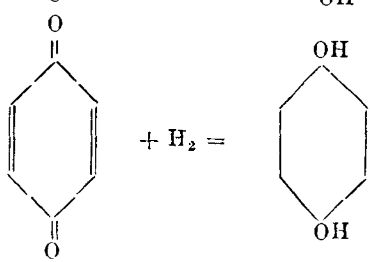
$$C_6H_4(NH_2)(COONa)[1{:}2] \xrightarrow{CH_2(OH)(SO_3Na)} CH_2(SO_3Na)NH.C_6H_4COONa[1{:}2]$$

$$\xrightarrow{KCN} CH_2(CN)NH.C_6H_4COONa[1{:}2] \xrightarrow{CH_3COOH} CH_2(CN)NH.C_6H_4COOH[1{:}2]$$

*Yield.*—Theoretical (18 gms.). Crystallises from alcohol (3 parts) in leaflets ; from benzene or chloroform in long needles ; insoluble in water ; M.P. 183°. (D.R.P., 157909 ; B., 39, 2807.)

**Reaction L.** (*c*) **Action of Hydrogen Cyanide on Quinones.** (B., 33, 675 ; D.R.P., 117005.)—Hydrogen cyanide reacts easily with quinones to give dicyano-dihydroxy derivatives of the parent hydrocarbons. A molecule of the quinone is simultaneously reduced.




Preparation 88.—**Dicyanoquinol** (1 : 4-*Dihydroxy*-2 : 3-*dicyanobenzene*).


$C_8H_4O_2N_2$. 160.

(*This preparation must be carried out in a fume cupboard.*)

20 gms. (2 mols.) of *p*-benzoquinone are dissolved in 60 c.cs. of alcohol,

and a cold mixture of 25 c.cs. (excess) of conc. sulphuric acid and 50 c.cs. of alcohol are added. The mixture is well cooled in a freezing mixture, and a 50% solution of potassium cyanide (*caution !*) slowly run in until a green fluorescence appears, and the liquid reacts alkaline. About 110 gms. of solution will be required. The whole is then acidified with sulphuric acid (*caution !*) and the alcohol removed by distillation under reduced pressure from a water bath. The residue is washed with water, and recrystallised from hot water with the addition of animal charcoal.

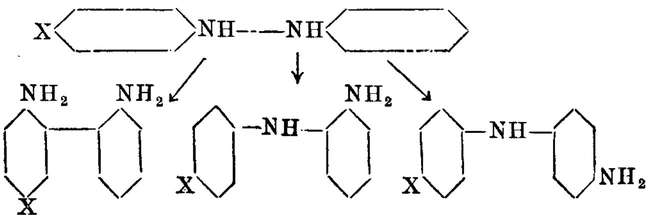
$$2C_6H_4O_2 + 2HCN = C_6H_2(OH)_2(CN)_2[1:4:2:3] + C_6H_4(OH)_2[1:4].$$

Crystallises in pale yellow leaflets, which contain 2 mols. of water; slightly soluble in water; its neutral solution fluoresces blue, its acid solution violet, and its alkaline solution green; on heating it decolorises at 230°. (B., 33, 675; D.R.P., 117005.)

**Reaction LI.** (*a*) **Action of Acids on the non-para substituted Hydrazo Compounds.** (A., 270, 330; 287, 97; B., 26, 681, 688, 699.)—When hydrazobenzene is treated with mineral acids, an intermolecular rearrangement to benzidine ($p_1$-$p_2$-diaminodiphenyl) takes place.

$$C_6H_5.NH.NH.C_6H_5 \rightarrow H_2N.C_6H_4.C_6H_4NH_2[4:4'].$$

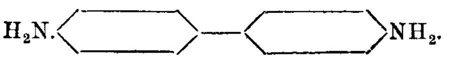
This reaction can be extended to almost all non-*para* substituted hydrazo compounds; if one or both *para*-positions are substituted, either *ortho*-benzidine or diphenylamine derivatives known as *ortho*- or *para*-semidines are formed.




*o*-Benzidine. *o*-Semidine. *p*-Semidine.

Benzidine and its homologues are very important intermediates in the dye industry.

PREPARATION 89.—**Benzidine** (4 : 4′-*Diaminodiphenyl*).




$C_{12}H_{12}N_2$. 184.

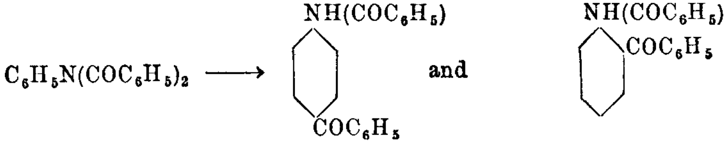
5 gms. hydrazobenzene are slowly heated to boiling in a narrow-necked flask, with 6 c.cs. conc. hydrochloric acid in 50 c.cs. water, a crystal of sodium bisulphite being added occasionally to minimise oxidation of the hydrazobenzene. The solution at the boil should be acid to Congo red (test). The hot solution is filtered from insoluble matter (azobenzene), and a saturated solution of sodium sulphate added until the benzidine sulphate is completely precipitated (test). The sulphate is then filtered and washed free from acid with hot water. The moist sulphate is removed, heated with stirring to 50° with a little water, and caustic soda solution

added until an alkaline reaction to phenolphthalein is obtained. When cold, the free base is filtered, dried at 50°, and crystallised from benzene, alcohol or hot water. From the last solvent, it crystallises under certain conditions as the monohydrate. (See p. 490.)

$$C_6H_8NH.NH.C_6H_5 \longrightarrow H_2N.C_6H_4C_6H_4NH_2[4:4'].$$

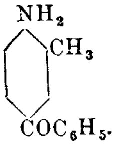
*Yield.*—90% theoretical (4·5 gms.). Lustrous plates when freshly crystallised; M.P. 127°; darkens in air; soluble in hot water; forms monohydrate, M.P. 105°; forms a difficultly soluble sulphate. (J. pr., [1], 36, 93.)

**Reaction LI.** (*b*) **Molecular rearrangement of Dibenzanilides.**—When dibenzanilide is heated at 230° for 2 days, rearrangement takes place, and 2- and 4-(benzoylamino)-benzophenones are formed.




If either the *o*- or *p*-position is occupied, only one isomer is obtained; transformation to the *meta*-position does not occur. This is a standard method of preparation of acyl-amino-ketones, or by a further hydrolysis of amino-ketones. The tendency, illustrated in this reaction, of groups to wander from the amino group to the nucleus, is also shown in previous reactions and in the preparation of aminoazobenzene from diazoaminobenzene (Preparation 456), of sulphanilic acid from aniline sulphate (Preparation 292), of *o*- and *p*-chloroacetanilides from acetochloranilide (Preparation 328), of *o*- and *p*-toluidine from methylaniline hydrochloride, and of 1 : 2 : 4-aminodimethylbenzene (2 : 4-xylidine) from dimethylaniline hydrochloride.

PREPARATION 90.—**4-Amino-3-methylbenzophenone**) (*1-Methyl-3-benzoyl-6-aminobenzene*).




$C_{14}H_{13}ON$. 211.

To 26 gms. (2 mols.) of benzoyl chloride are added gradually 10 gms. of *o*-toluidine (1 mol.) and the mixture is heated for 15 hours in an oil bath at 230°. A brown viscid liquid is formed which solidifies on cooling. In order easily to separate the 4-amino-3-methylbenzophenone, the mass is hydrolysed by boiling for 14 hours with excess of alcohol containing half its bulk of conc. hydrochloric acid. The product thus obtained is steam distilled when alcohol and then ethyl benzoate pass over. The acid residue which contains the hydrochloride of the base is boiled for some time with water and filtered from tarry matter. The filtrate is then made slightly alkaline, and *o*-toluidine derived from untransformed dibenzoyl-

*o*-toluidine, removed by steam distillation. A solid separates from the alkaline liquid in the flask, and after cooling this is filtered off and extracted with absolute alcohol. The alcohol is almost completely removed on the water bath, and a few drops of conc. sulphuric acid are added. On adding a little ether, the base crystallises out in the form of colourless needles.

$$CH_3.C_6H_4.NH_2[1:2] + 2C_6H_5COCl \longrightarrow CH_3C_6H_4.N(COC_6H_5)_2 + 2HCl$$

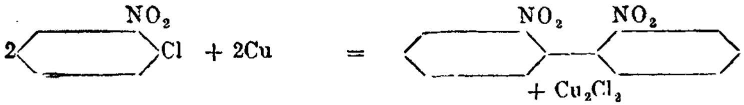
$$CH_3C_6H_4N(COC_6H_5)_2 \longrightarrow CH_3.C_6H_3(COC_6H_5)NH(COC_6H_5) \quad [1:5:2]$$

$$\xrightarrow{HCl + C_2H_5OH} CH_3.C_6H_3.(COC_6H_5)NH_2.HCl + C_6H_5COOC_2H_5$$

$$\xrightarrow{NaOH} CH_3.C_6H_3.(COC_6H_5)NH_2 \quad [1:5:2].$$

Colourless needles; M.P. 112°, soluble in alcohol; insoluble in ether and in water. (J. C. S., 85, 386, 591.)

**Reaction LII.** (*a*) **Action of Copper Powder on 2- and 4-mono-nitro- and 2 : 4-di-nitro-chloro- and -bromo-benzenes and their Homologues** (Ullmann). (B., 34, 2172.)—Symmetrical diphenyl derivatives can be prepared from aromatic iodo-compounds and copper powder (see Reaction VII. (*b*)). Chloro- and bromo-compounds, however, only react when activated by nitro groups in the *ortho*- or *para*-positions. Di-nitro-diphenyl derivatives can be obtained from them in good yield by heating with the metallic powder to about 250° in sealed tubes. If both the *ortho*- and *para*-positions are occupied by nitro groups, the activation of the halogen atom is such that the corresponding diphenyl derivative can be prepared by boiling with copper powder in nitrobenzene. (J. C. S., 1931, 3176.)




PREPARATION 91.—**2 : 2′ : 4 : 4′-Tetranitrodiphenyl.**

$[2{:}4](NO_2)_2C_6H_3.C_6H_3(NO_2)_2[2'{:}4']$. $C_{12}H_6O_8N_4$. 334.

10 gms. (1 mol.) of 2 : 4-dinitrochlorobenzene (see p. 273), 10 gms. (excess) of copper powder, and 20 c.cs. of nitrobenzene are refluxed for 1 hour and the cooled solution diluted with ether and filtered. Ligroin is slowly added to the filtrate and the oil which separates crystallised by scratching the sides of the vessel. It is recrystallised from benzene.

$$[1:2:4](NO_2)_2C_6H_3Cl + 2Cu + ClC_6H_3(NO_2)_2[1:2:4] =$$
$$[2:4](NO_2)_2C_6H_3.C_6H_3(NO_2)_2[2':4'] + Cu_2Cl_2.$$

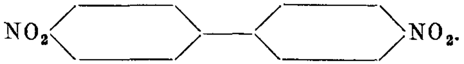
*Yield.*—66% theoretical (5·5 gms.). Yellowish prisms; insoluble in petroleum ether; M.P. 163°. (B., 34, 2177.)

**Reaction LII.** (*b*) **Action of Cuprous Chloride on Nitro-diazonium Compounds.** (B., 34, 3802; 38, 725.)—Ordinarily when cuprous chloride acts on a diazonium salt in acid solution, a chloro-compound is the chief product (Sandmeyer's reaction, p. 345), and only a small quantity of the corresponding diphenyl compound is formed. But if a nitro-diazonium

salt be used, the diphenyl derivative is formed in much larger quantities. The same holds good for Gattermann's modification of the reaction using copper powder (B., 23, 1226).

$$2C_6H_4(NO_2)N_2Cl + Cu_2Cl_2 = (NO_2)C_6H_4.C_6H_4(NO_2) + 2CuCl_2 + 2N_2.$$

PREPARATION 92.—*p-p'*-**Dinitrodiphenyl.**



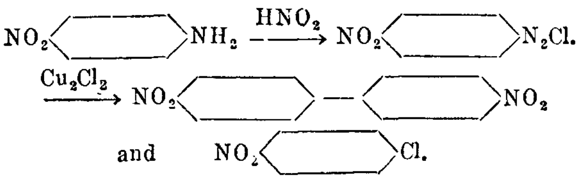

$C_{12}H_8N_2O_4$. 244.

*By-product:* *p*-**Chloronitrobenzene.** (*1-Chloro-4-nitrobenzene*)

$C_6H_4(Cl)(NO_2)[1:4]$. $C_6H_4O_2NCl$. 157·5.

A cold solution of 21·6 gms. (1 mol.) of cuprous chloride in 100 c.cs. of conc. hydrochloric acid (see p. 506) is added to the diazonium solution prepared from 30 gms. (1 mol.) of *p*-nitroaniline, 45 gms. (excess) of conc. sulphuric acid, 60 c.cs. of water and 15·3 gms. (1 mol.) of sodium nitrite (p. 374).

During the addition of the copper salt the whole is vigorously stirred. There is a brisk evolution of nitrogen, the mass turns black and a brownish-yellow substance is precipitated. When the liquid becomes green, the reaction is finished. The product is distilled in steam until no more *p*-chloronitrobenzene passes over. There remains in the distilling flask almost pure 4 : 4'-dinitrodiphenyl. It is filtered off, dried, and re-crystallised from benzene. The by-product *p*-chloronitrobenzene is worked up by filtering it from the liquid portion of the distillate, drying on a porous plate, and recrystallising from benzene.



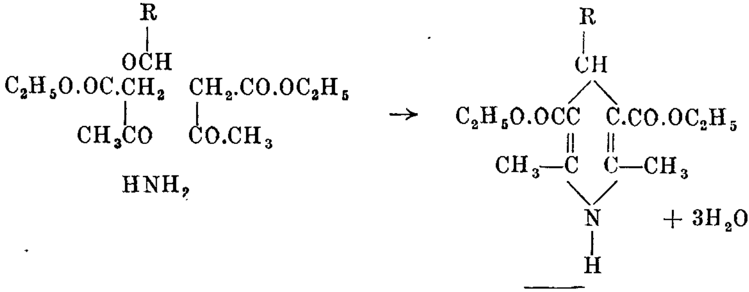

*Yield.*—4 : 4'-*dinitrophenyl* 55% theoretical (14 gms.); *p-chloronitrobenzene* 40% theoretical (13 gms.). 4 : 4-*dinitrodiphenyl* is a crystalline solid; M.P. 237°; *p-chloronitrobenzene* is a crystalline solid; M.P. 83°; B.P., 238·5°. (B., 38, 726.)

In an exactly analogous manner there is obtained from 30 gms. of *m*-nitroaniline, 23 gms. (87%) of 3 : 3'-dinitrodiphenyl (yellow needles; insoluble in cold glacial acetic acid; M.P. 200°) and 6 gms. (20%) of *m*-chloronitrobenzene (colourless crystals; insoluble in cold benzene; M.P. 45°; if rapidly cooled after fusion, melts at 24°, but in a short time reverts to the stable modification). (O. S., IX., 92.)

Similarly 30 gms. of *o*-nitroaniline yield 17·6 gms. (64%) of 2 : 2'-dinitrodiphenyl (crystalline solid, insoluble in cold benzene; M.P. 127°) and 9 gms. (30%) of *o*-nitrochlorobenzene (colourless crystals, insoluble in cold benzene; M.P. 32·5°).

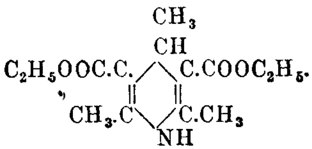
**Reaction LIII. Action of Ethyl Acetoacetate on Aldehyde-ammonias** (Hantzsch). (A., 215, 1.)—When acetoacetic ester is heated with

aldehyde ammonias alkyl derivatives of dimethyldihydropyridinedicarboxylic ester are produced.



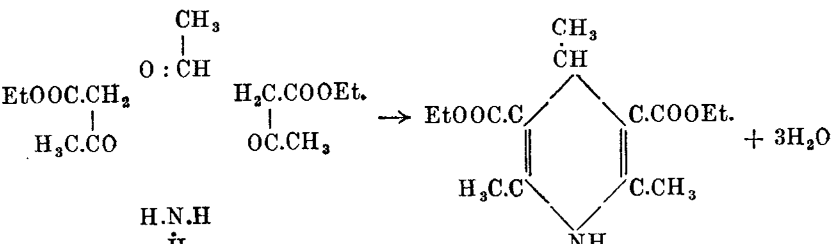
A great many aldehydes can be employed—propaldehyde, nitrobenzaldehyde, phenylacetaldehyde, furfurol—so that the reaction is of wide application. For the steps in the conversion of the compounds obtained to alkyl or aryl derivatives of dimethylpyridine, see pp. 242, 411, 412.

PREPARATION 93.—**Diethyldihydrocollidinedicarboxylate** [2 : 4 : 6-*Trimethyl*-3 : 5-*dicarbethoxy-piperidine*-(2)-(5)-*di-en*].



$C_{14}H_{21}O_4N$. 267.

13 gms. (slightly more than 1 mol.) of acetaldehyde-ammonia (see p. 416) are covered with 80 gms. (2 mols.) of ethyl acetoacetate and warmed gently (in a fume cupboard) until ebullition has commenced (100°—110°, stir with a thermometer). Should the reaction become too violent, the heating is stopped until it subsides. In 5 minutes the reaction is completed, and an equal volume of dilute hydrochloric acid is added with stirring to the hot liquid, the stirring being continued until the oil which separates sets to a white crystalline mass. This latter is powdered, filtered, washed first with diluted hydrochloric acid and then with water, well pressed, and recrystallised from the minimum quantity of hot alcohol.



*Yield.*—66% theoretical (30 gms.). Colourless plates with bluish fluorescence ; insoluble in water ; sparingly soluble in alcohol, ether, and carbon disulphide ; readily soluble in benzene ; M.P. 131°. (A., 215, 1.)

**Reaction LIV.** (*a*) **Condensation of Non-di-ortho-substituted-primary-**

**aromatic Amines with Acrolein** (Skraup). (M., 1, 316; 2, 141; B., 13, 911; 14, 1002; 29, 705.)—When a primary aromatic amine which has a non-substituted carbon in the *ortho*-position is heated with glycerol and conc. sulphuric acid in the presence of an oxidising agent, the following series of reactions occurs:—

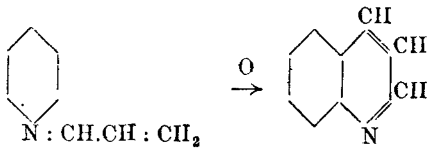
(i.) The glycerol is dehydrated by the acid to acrolein.

$$CH_2OH.CHOH.CH_2OH \xrightarrow{-2H_2O} CH_2 = CH.CHO.$$

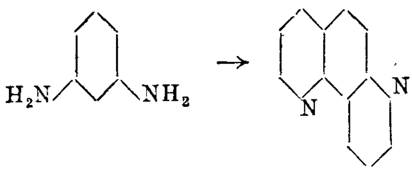
(ii.) The aldehyde then condenses with the aromatic amine to form an anil.

$$CH_2 : CH.CHO + RNH_2 \rightarrow CH_2 : CH.CH : NR + H_2O.$$

(iii.) The latter compound under the influence of the oxidising agent condenses to a derivative of quinoline.

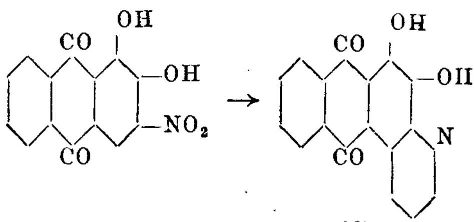


The oxidising agent usually employed is the nitro-compound corresponding to the amine, *e.g.*, nitrobenzene when aniline is the base; for *p*-toluidine, *p*-nitrotoluene serves, and so on. Arsenic acid, however, can be generally employed, and gives better results. The reaction is capable of very wide application; nitro-, halogen-, hydroxy-, carboxy-quinolines can all be obtained from the corresponding amines; the amino-naphthalenes also react. Diamines yield the so-called phenanthrolines. (B., 16, 2519; 23, 1016.)



*m*-Phenanthroline.

Sometimes the amine can be dispensed with, and the corresponding nitro-body used alone. It is reduced by the hydrogen arising in the reaction. Of technical interest is the fact that $\beta$-nitro-alizarin on heating with glycerol and sulphuric acid yields a blue dye—Alizarin Blue. (B., 16, 445; 29, 708; A., 201, 333.)

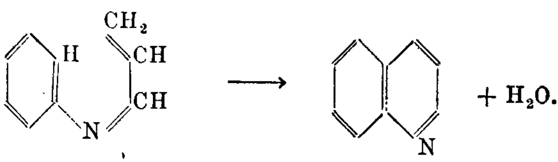


Alizarin Blue.

PREPARATION 94.—**Quinoline** (*Benzpyridine*).

$C_9H_7N$. 129.

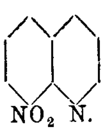
125 gms. of conc. sulphuric acid are gradually added, with shaking, to a mixture of 46 gms. (1 mol.) of aniline, 30 gms. of nitrobenzene, 125 gms. (excess) of glycerol, and 12 gms. of ferrous sulphate, contained in a 2-litre round-bottomed flask. The latter is fitted with a long wide reflux condenser, and heated on a sand bath until white vapours are evolved. Heating is discontinued until the reaction moderates, when the flask is again heated to gentle ebullition for 5 hours. Water is added, and the unchanged nitrobenzene distilled off in steam. The residue is treated with conc. caustic soda solution until it is strongly alkaline, and the quinoline and aniline present distilled off in steam. The distillate is treated with dilute sulphuric acid until the bases are both completely dissolved and the solution contains *excess* of acid. To the cooled solution sodium nitrite solution is added until a drop of the solution gives a blue coloration with potassium-iodide-starch paper (see p. 373). The aniline is thus converted into the diazonium compound, and on boiling on a water bath the latter passes into phenol. The solution is again made alkaline, and the quinoline distilled off in steam. The distillate is extracted with ether, dehydrated over solid caustic potash, the ether removed on a water bath, and the residue distilled.



*Yield.*—80% theoretical (50 gms.). Colourless liquid; B.P., 237°; $D^0_4$ 1·108. Am. Soc., 50, 2709; O. S., II., 79.

It is claimed that the presence of boric acid reduces the violence of the reaction (Am. Soc., 52, 3685; E.P., 394416).

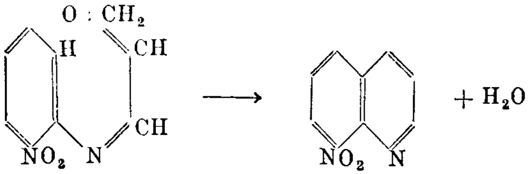
PREPARATION 95.—**8-Nitroquinoline** (*o-Nitrobenzpyridine*).



$C_9H_6O_2N_2$. 174.

100 gms. of conc. sulphuric acid and 51·5 gms. of arsenic acid are well shaken in a flask with 110 gms. glycerine and 50 gms. of *o*-nitroaniline and then carefully heated on a sand bath under a reflux condenser. As soon as the reaction begins, the flask is removed from the sand bath until it has moderated; it is then boiled for 3 hours. When cold, a large volume of water is added to the contents of the flask, and the whole allowed to stand overnight, and then filtered. Caustic soda is carefully added to the

filtrate until a brown precipitate appears, which is filtered off and discarded. Caustic soda is then added to the filtrate until alkaline. The nitro-quinoline thus obtained is washed with water, boiled up with alcohol and animal charcoal, and after filtration is precipitated by the addition of water.




*Yield.*—55% theoretical (35 gms.). Colourless monoclinic needles; insoluble in water; soluble in alcohol; M.P. 88°. (B., 29, 705.)

**Reaction LIV.** (*b*) **Condensation of Primary Aromatic Amines, other than Ortho Substituted, with two Molecules of certain Aldehydes** (**containing the group—$CH_2CHO$**) **under the influence of Sulphuric or Hydrochloric Acid.** (B., 16, 2415; A., 249, 110.)—Quinolines substituted in the benzene or in both nuclei may be formed, anils being formed intermediately.

$$R_1NH_2 + OHC.CH_2.R \rightarrow R_1N : CH.CH_2R.$$

Two molecules of the latter then combine to give

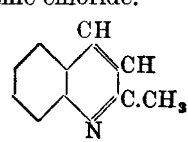
$$\begin{array}{l} R_1N = CHCHR \\ \quad R_1NH.CH \\ \qquad\quad CH_2R \end{array}$$

which splits off amine and hydrogen to give a quinoline derivative (B., 29, 59).

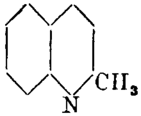
$$(R_1 - H)\begin{cases} ^{[1]}CH = CR \\ ^{[2]}N \;\; = CCH_2R. \end{cases}$$

That hydrogen is set free is proved by the reduction of some of the quinoline derivative to a tetrahydroquinoline derivative. A mixture of two aldehydes, or of an aldehyde and a ketone, may be employed. (B., 20, 1098.)

An alkylidene-aniline may be substituted for the primary amine, and the condensation takes place in presence of zinc chloride.

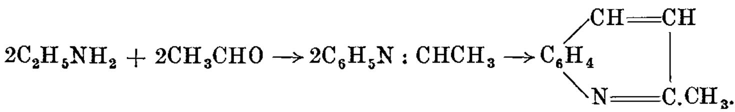
$C_6H_5N : CHCH_3 + CH_3CHO \rightarrow$ 


PREPARATION 96.—**Quinaldine** (2-*Methylquinoline*).



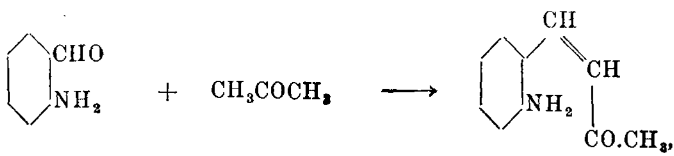

$C_{10}H_9N$. **143.**

To a mixture of 30 gms. conc. hydrochloric acid and 10 gms. zinc chloride are added 51 gms. (1 mol.) of aniline, and the whole is refluxed on a water bath. To this is slowly added during 2 hours, $12\frac{1}{2}$ gms. (2 mols.) of acetaldehyde. The whole is boiled on a sand bath for 90 minutes, and after making alkaline with caustic soda, is steam distilled. The quinaldine is separated and distilled, the fraction 244°—250° being collected.

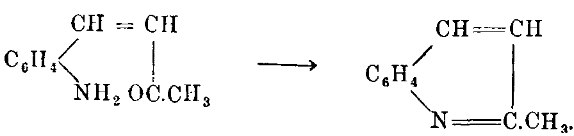


*Yield.*—50% theoretical (6 gms.). Colourless liquid; characteristic odour; insoluble in water; B.P. 247°. (B., 16, 2465; E.P., 395063.)

**Reaction LIV.** (*c*) **Condensation of *o*-Aminobenzaldehydes with Aldehydes, Ketones, Ethyl acetoacetate, etc., under the influence of a trace of Sodium Hydroxide, to give Quinoline Derivatives** (B., 16, 1835; 25, 1752).—The first stage is the formation of an *o*-aminostyryl ketone.



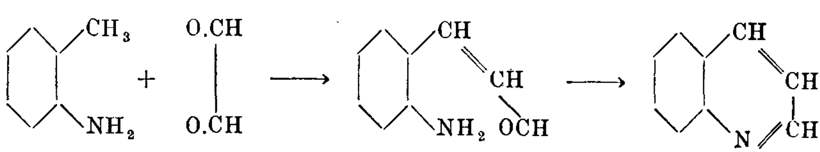
which, like all such compounds, readily condenses to a quinoline derivative.



The reaction usually takes place by gentle warming with a trace of alkali in alcoholic solution.

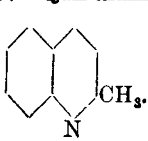
$\gamma$-Hydroxy-quinolines may be prepared by condensing anthranilic acid with aldehydes, ketones, etc. (B., 28, 2809.)

An interesting synthesis of quinoline from *o*-toluidine is given by condensation with glyoxal (B., 27, 628).



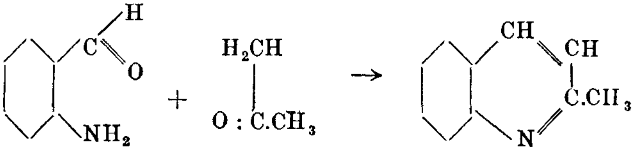
*Cf.* the synthesis of Carbostryl, B., 14, 1916.

PREPARATION 97.—**Quinaldine** (2-*Methylquinoline*).



$C_{10}H_9N$. 143.

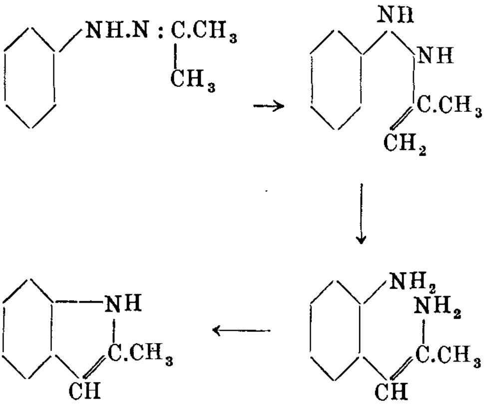
20 gms. (1 mol.) of *o*-amino-benzaldehyde and 9 gms. (1 mol.) of dried and redistilled acetone are dissolved in absolute alcohol, and a few drops of alcoholic caustic soda added. The condensation takes place at ordinary temperature. The quinaldine is distilled off in steam and washed with water until free from acetone.



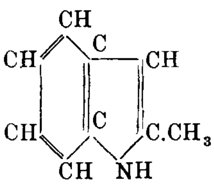
*Yield.*—Theoretical (23 gms.). Colourless liquid; insoluble in water; B.P. 247°. (B., 16, 1834.)

**Reaction LV. Intramolecular condensation of Phenylhydrazones of Aldehydes, Ketones and Ketonic Acids by heating with Hydrochloric Acid or Zinc Chloride** (Fischer). (B., 19, 1563; 26, R., 14; E.P., 385605.)—This is an important method of preparation for the alkylindols. The reactions occurring are somewhat complicated, since both a rearrangement and the elimination of ammonia take place.

Robinson (J. C. S., 113, 639; 125, 827) has put forward the hypothesis that the fundamental reactions involved are, in succession, a rearrangement to an unsaturated hydrazine, an isomeric change of the *o*-benzidine type, and finally the elimination of ammonia from the resulting diamine:



PREPARATION 98.—**2-Methylindole** (*Methylketole*).



$C_9H_9N$. 131.

30 gms. (1 mol.) of phenylhydrazine are mixed with 18 gms. (slightly more than 1 mol.) of commercial acetone (B.P., 56°—58°). The mixture

becomes very warm and a good deal of water separates. The mixture is heated on a water bath for 15 minutes, a small portion being occasionally tested with Fehling's solution. As long as phenylhydrazine is present in excess, the Fehling's solution is reduced; more acetone is then added from time to time until the reducing action of the mixture has almost ceased. The turbid oil (crude acetone-phenylhydrazone) is placed in a large copper crucible, and the excess of acetone removed by heating on a water bath for $\frac{1}{2}$ hour. 200 gms. of dry commercial zinc chloride are next added, and the mixture heated on the bath with frequent stirring. The whole is then heated on an oil bath to 180°, and, when in a few minutes the mass has acquired a dark colour, the crucible is immediately removed from the bath and stirred. The reaction is complete in a short time, and can be followed by the change in colour of the fusion and the evolution of vapours. The dark fused mass is treated with $3\frac{1}{2}$ times its weight of hot water, and distilled in steam after acidification with a little hydrochloric acid. The methylketole distils over, slowly but completely, as a pale yellow oil which soon solidifies. This is filtered off, melted to free it from water and distilled. It must be kept in a well-closed bottle.

*Yield.*—55% theoretical (20 gms.). Pale yellow crystals; obnoxious odour; M.P. 59°; B.P. $^{750}$ 272°. (A., 234, 126.)

# CHAPTER IX

## THE LINKING OF HYDROGEN TO CARBON

### Hydrogen Compounds

Although neither so numerous nor important as the carbon to carbon reactions discussed in Chapter VIII., a number of reactions, more particularly those classed under the heading of reductions, are dealt with below. Some of the most important methods of preparing hydrocarbons depend on the reduction of derivatives previously obtained.

**Reaction LVI. Action of Water on certain Metallic Carbides.** (J. C. S., 87, 1232.)—This reaction has an important and well-known application in the production of acetylene on an industrial scale. Methane can be obtained in a similar way from aluminium carbide.

$$Ca\left\langle\begin{matrix}C\\ |||\\ C\end{matrix}\right. + 2H_2O = Ca(OH)_2 + \begin{matrix}CH\\ |||\\ CH.\end{matrix}$$

$$Al_4C_3 + 12H_2O = 3CH_4 + 4Al(OH)_3.$$

Preparation 99.—**Acetylene** [*Ethin*].

$$\begin{matrix}CH\\ |||\\ CH.\end{matrix} \qquad C_2H_2. \qquad 26.$$

10 gms. of calcium carbide are placed in a shallow layer over sand in a large conical flask fitted with a two-holed rubber stopper carrying a tap funnel and a delivery tube. Water is added drop by drop from the tap funnel. The gas evolved contains sulphuretted hydrogen, hydrogen from free calcium, siluretted hydrogen from calcium silicide, phosphoretted hydrogen from calcium phosphide, and acetaldehyde vapour produced by condensation of acetylene with water. The gas is purified by passing it through (i.) dilute sulphuric acid; this removes ammonia; (ii.) a tower packed with a mixture of equal parts of bleaching powder and quicklime; this removes phosphorus compounds; (iii.) a solution of cupric chloride acidified with dilute sulphuric acid; (iv.) a solution of ferric chloride similarly acidified; (v.) a solution of chromic acid; all these remove phosphorus and sulphur compounds; (vi.) a 50% aqueous solution of caustic potash. The gas is collected in a gas-holder, over 50% aqueous glycerol, in which it is only very slightly soluble. Before collecting, care should be taken that all air has been removed from the apparatus; during the filling of the holder the rate of flow of liquid from it should be adjusted so that there is a slightly increased

pressure in the apparatus; this can be seen from the height of liquid in the central tube of the gas-holder.

The purity of the gas is tested by explosion analysis (J. C. S., 84, 555); the ratio, contraction on explosion to absorption by baryta water after explosion, should lie between 0·73 and 0·77 (theoretical 0·75). Great care must be taken that this preparation is carried out in the absence of flame, and that neither the apparatus nor the collected gas is exposed to direct sunlight, which decomposes acetylene. Also the cupric chloride solution employed for washing should be kept acid; if it becomes alkaline the explosive copper acetylide is precipitated. Should this occur the solution is mixed with much water and poured away.

$$CaC_2 + 2H_2O = C_2H_2 + Ca(OH)_2.$$

Colourless gas; when pure has a garlic-like smell; at N.T.P. water dissolves 1 volume; acetone 31 volumes; explosive limits in air 3—52%; in oxygen 2—92%. (J. C. S., 87, 1232.)

Methane is prepared from aluminium carbide and dilute hydrochloric acid in a similar apparatus. It is purified as described on p. 182.

**Reaction LVII. Action of Hydrogen in the presence of finely divided Nickel on Aromatic Compounds** (Sabatier-Senderens). (C. r., 132, 210.)—The addition of hydrogen to an aromatic compound by passing its vapour mixed with hydrogen over finely divided nickel at a relatively low temperature is a reaction of wide and important application. Although nickel is the metal most usually employed, other metals can also act as hydrogen carriers. The method is chiefly used for the reduction of the nucleus in aromatic compounds—hydrocarbons, phenols, amines, etc., to the corresponding unsaturated and fully saturated paraffin derivatives. Ethylenic and acetylenic linkings, aldehydes and ketones can be reduced. The reaction has been applied on a large scale to the hydrogenation ("hardening") of fats and oils.

Raney nickel (Am. Soc., 54, 4116) is particularly reactive for hydrogenation in the liquid phase at low temperatures and pressures, whilst nickel-kieselguhr (*loc. cit.* 1651) is suitable for various types of hydrogenation at high pressures.

PREPARATION 100.—**Hexahydrobenzene** (*Cyclohexane*).

$C_6H_{12}$. 84.

## Preparation of the Catalyst

Small pieces of pumice stone of a convenient size are soaked in a concentrated solution of nickel nitrate in distilled water, and heated in a basin over a free flame until the nitrate has been converted into the oxide. Alternatively the pumice is impregnated with a paste of its own weight of nickel oxide and distilled water, and dried on a water bath. The nickel oxide is reduced by heating in a current of pure, thoroughly dried hydrogen in a combustion tube. The arrangement of the apparatus and the preparation and purification of hydrogen are the same as for the prepara-

tion of reduced copper (see p. 418). The pumice is loosely packed into the combustion tube and kept in position by asbestos plugs. The air bath is maintained at about 280° ; it is tilted slightly forwards so that any liquid formed may run down into the receiver. Ordinary corks should be used, and not rubber stoppers, in making the connections to the combustion tube. Unpurified hydrogen must not be admitted, as otherwise the catalyst will be poisoned. It is convenient to have a by-pass in the form of a T-piece between the copper gauze and the caustic soda tower.

At first the hydrogen escapes through the by-pass. After the air has been expelled (a sample must be collected and tested) as far as the T-piece, the copper gauze tube is heated, and the current of hydrogen is then diverted through the tower into the combustion tube. Some should also be allowed to escape through the funnel B (Fig. 51) to remove air from its stem. When the air has been expelled completely, the air bath carrying the combustion tube is heated. Air must not be allowed to enter the combustion tube from this until the end of the experiment. The reduction of the nickel oxide will take at least a week ; the hydrogen is passed at the rate of about 300 c.cs. per minute. The reduction is accompanied by a colour change from black to a greyish-yellow, and is complete when no more steam is evolved, *i.e.*, when a calcium chloride tube at the exit end of the combustion tube does not gain in weight after passing the exit gas through it for $\frac{1}{4}$ hour.

### Hydrogenation of Benzene

The benzene used should first be tested for thiophene with isatin and conc. sulphuric acid, and then redistilled and recrystallised ; traces of

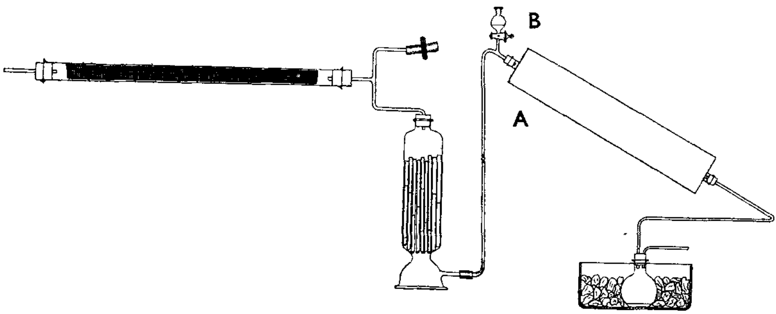



FIG. 51.

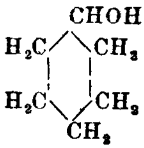
sulphur and chlorine compounds completely inhibit the reaction. The benzene is passed at the rate of about 7 c.cs. per minute into the combustion tube by means of a dropping funnel, B, whose stem, drawn out to a capillary, passes through one hole of the double-holed cork at A (Fig. 51). The quantity of benzene used is obtained by weighing the amount in the funnel before and after the experiment. The temperature of the air bath should be 180°—190°, and the hydrogen should be passed at about

250 c.cs. per minute. When commencing to add the benzene at A, air must not be allowed to enter the tube; the vapour issuing from the combustion tube is condensed in a flask immersed in a freezing mixture. The condensate contains some unchanged benzene. This, when 40 gms. or more have been collected, is treated with a nitrating mixture of sulphuric and nitric acids (p. 269). Cyclohexane is scarcely affected by this mixture while benzene is rapidly nitrated. It cannot otherwise easily be separated from cyclohexane; their boiling points and freezing points are almost identical. After standing for 1 hour the top layer of oil is separated, well washed with water, and dried for 24 hours over calcium chloride. It is fractionated, and the fraction 78°—85° redistilled and collected between 80°—82°.

$$C_6H_6 + 3H_2 = C_6H_{12}.$$

*Yield.*—80% theoretical. Calculated on the benzene volatilised (8·5 gms. cyclohexane per 10 gms. benzene). Almost theoretical allowing for unchanged benzene (11 gms. cyclohexane per 10 gms. benzene). Colourless liquid; insoluble in water; B.P. 81°. (C. r., 132, 210.)

PREPARATION 101.—**Hexahydrophenol** (*Cyclohexanol*).



$C_6H_{12}O$. **100.**

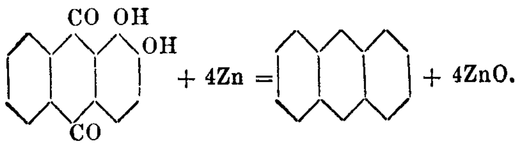
The apparatus is as in Preparation 100, except that in front of the catalyst tube is inserted a small distilling flask weighed before and after the experiment containing 100 gms. of pure redistilled phenol. Hydrogen enters by means of a one-holed cork in the neck of the flask and leaves by the side tube, which fits into a one-holed cork at A (Fig. 51). During the reduction (p. 172) of the nickel oxide the tube by which the hydrogen enters the flask is raised a little above the surface of the phenol. After reduction is complete and the temperature of the catalyst has been reduced to 180°—190°, the phenol in the flask is heated almost to its boiling point, and the hydrogen delivery tube pushed well down into the liquid. Care must be taken that phenol does not condense in the tube, and that only the vapour passes over. When sufficient liquid has condensed in the receiver, it is shaken with caustic soda solution to remove unchanged phenol, extracted with ether, and the extract dried over anhydrous potassium carbonate for 24 hours. The ether is removed on a water bath, and the residue distilled; the fraction 156°—164° is collected and refractionated between 159°—161°.

$$C_6H_5OH + 3H_2 = C_6H_{11}OH.$$

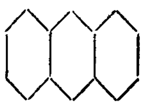
*Yield.*—Almost theoretical (10·5 gms. of hexahydrophenol per 10 gms. of phenol). Colourless liquid; aromatic smell, insoluble in water; B.P. 161°. (C. r., 132, 210.)

Hexahydrotoluene, hexahydrocresol, etc., may be obtained by methods exactly similar to the foregoing.

**Reaction LVIII.** (*a*) **Reduction of Phenols and Quinones by Distillation with Zinc Dust.** (A., 140, 205.)—When certain aromatic oxygen compounds (phenols, naphthols, quinones, etc.), are heated with zinc dust, they are reduced to the corresponding hydrocarbons. Thus, phenol yields benzene, the naphthols naphthalene; while anthracene can be obtained from anthraquinone or its hydroxy derivatives, alizarin, or quinizarin. In this way alizarin was first proved to be an anthracene derivative. (B., 1, 43.) For catalytic reduction of phenols, see C. r., 193, 1023.



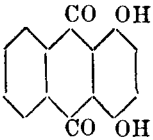
PREPARATION 102.—**Anthracene** (*s-Dibenzbenzene*).



$C_{14}H_{10}$. 178.

Pieces of porous pumice stone of a size that will conveniently pass into a combustion tube are added to a paste prepared from 100 gms. of good zinc dust and 30 c.cs. of alcohol. The mixture is stirred to incorporate the pumice and paste. They are removed from the paste with tongs, and heated in a porcelain dish with constant motion over a free flame until the alcohol is evaporated. A hard glass combustion tube, 70 cms. long, is drawn out at one end to a narrow tube, the narrowed end is closed by a loose plug of asbestos, and a layer of zinc dust, 5 cms. long, is placed next to the plug, then a mixture of 2 gms. of quinizarin (see p. 108), alizarin, or anthraquinone with 20 gms. (excess) of zinc dust, and finally a layer of pumice zinc dust, 30 cms. long. After a canal has been formed over the zinc dust by placing the tube in a horizontal position and tapping it, the latter is transferred to a combustion furnace, tilted forwards, as in a nitrogen estimation (see p. 461), and a rapid current of dry hydrogen (see p. 418) is passed through the tube without heating. The open end of the tube is closed by a one-holed cork, and the issuing gas led to a draught pipe. After the gas has been passed for some time a test tube of the issuing gas is collected over water at intervals, and a light applied to the mouth of the test tube at least 12 ft. from the apparatus. When the contents of the tube burn quietly, all the air has been displaced from the apparatus. The gas current is then diminished to about 150 c.cs. per minute, and the pumice zinc dust is heated with small flames. (On no account must the apparatus be heated until all the air has been displaced.) The heating is gradually increased from the front backwards, until finally the tube is heated as strongly as possible. The rear layer of 5 cms. of zinc dust is next similarly heated, and when this glows,

the mixture of anthracene derivative and zinc dust is gradually heated, all being done as in the estimation of nitrogen. The anthracene formed condenses to crystals in the forward cool part of the tube. After the reaction is complete, a rapid current of hydrogen is passed while the tube is cooling; the part containing the anthracene, when cold, is broken off and the substance removed with a small spatula; it is purified by sublimation (see p. 31).



$$+ 5H_2 = C_6H_4\left<\begin{matrix}CH\\|\\CH\end{matrix}\right>C_6H_4 + 4H_2O.$$

*Yield.*—Almost theoretical (1·5 gms.). Colourless crystals; insoluble in water; soluble in warm benzene and in glacial acetic acid; M.P. 213°; B.P. 351°; M.P. of picrate, 138°. (A., 140, 205.)

It is better to use alcohol in making zinc dust paste, for if there is much oxide present in the dust a great deal of heat may be evolved on adding water, and much oxidation of the metal occur.

The following is one of the methods employed for the separation of pure anthracene from the coal tar fraction containing it. Carbazole and phenanthrene are the chief impurities present.

## Purification of Crude Anthracene

Crude anthracene (about 40%) is mixed in a vessel fitted with a mechanical stirrer, with 1½ times its weight of benzol; or solvent naphtha (90% at 160°); this specification means that 90% by volume distils up to 160°. Sodium nitrite to one-tenth of the weight of crude anthracene taken is dissolved in 10 times its weight of water, and sufficient 10% sulphuric acid (7·2 gms. for each 1 gm. of 10% nitrite) to decompose this quantity of nitrite is added to the benzol—anthracene mixture and the temperature maintained at 25°. The nitrite solution is then run in at such a speed that no red fumes escape. When all the solution has been added the mixture is filtered at the pump. The filtrate consists of two layers, one of sodium sulphate solution and one of solvent naphtha, or benzol containing the impurities such as nitroso-carbazol. The purified anthracene on the filter is washed with benzol or solvent naphtha; this latter on a large scale is used for the final treatment of a fresh lot of crude anthracene. The initial benzol or solvent naphtha, after separation from the aqueous solution, is recovered by distillation. The anthracene from this treatment will be about 80% pure. It may be purified to 95% by crystallising from heavy bases (pyridine, etc.), and is finally raised by sublimation and recrystallisation from benzol to 98%. (For the estimation of purity, see p. 497.) (C. T., 23, 8, 21; D.R.P., 122852.)

**Reaction LVIII.** (*b*) **Reduction of Aromatic Ketones to the corresponding Hydrocarbons by treatment with Hydriodic Acid or with Sodium in Alcoholic Solution.** (B., 7, 1624; 31, 999.)—Two methods for the

reduction of aromatic ketones to the corresponding hydrocarbons are exemplified below. Method I. using hydriodic acid is a standard method for the reduction, especially the complete reduction, of an organic compound; the sodium-alcohol method given in II. is not so universally applicable—it is a milder reducing agent and more selective; thus, it was used by Bamberger in his researches on the formula of naphthalene, to reduce one only of the two rings in that compound and its derivatives. The nickel oxide-hydrogen method can be applied here, as also to the reduction of mixed aliphatic-aromatic ketones; aliphatic ketones are best directly reduced by Method I.

PREPARATION 103.—**Diphenylmethane** (*Benzylbenzene*).

$$C_6H_5.CH_2C_6H_5. \qquad C_{13}H_{12}. \qquad 168.$$

*Method I.*—10 gms. (1 mol.) of benzophenone, 12 gms. (nearly 2 mols.) of hydriodic acid (B.P. 127°) and 2 gms. (more than 1 atom) of red phosphorus are heated together in a sealed tube for 6 hours at 160° (see p. 41). The reaction mixture is extracted with ether and the extract washed with water several times. It is then filtered, dried over calcium chloride for 24 hours, the ether removed on a water bath and the residue distilled.

$$C_6H_5.CO.C_6H_5 + 4HI = C_6H_5.CH_2.C_6H_5 + H_2O + 2I_2.$$

*Yield.*—Theoretical (9 gms.). (B., 7, 1624.)

*Method II.*—10 gms. (1 mol.) of benzophenone are refluxed with 100 gms. (excess) of alcohol, and 10 gms. (excess) of sodium wire are gradually added through an addition tube (see p. 50) to the boiling liquid. When the solution of the sodium is complete, the liquid in the flask is cooled, saturated with carbon dioxide, poured into cold water and the whole extracted with benzene. The extract is dried for 24 hours over calcium chloride, the benzene removed on a water bath, and the residue distilled under reduced pressure, the fraction 174°—176° at 80 mms. being retained.

Almost theoretical (8·5 gms.). Colourless oil; orange like odour, solidifies to needle-shaped crystals; M.P. 26°; B.P. $^{760}$ 263°; B.P. $^{80}$ 175°. (B., 31, 999.) For catalytic hydrogenation of ketones, see B., 66, 873.

**Reaction LVIII.** (*c*) **Reduction of the Carbonyl to the Methylene Group by means of Zinc Amalgam and Hydrochloric Acid** (Clemmensen). (B., 46, 1837; 47, 51; 47, 681.)

Aliphatic aldehydes and ketones and also aliphatic-aromatic ketones can be converted into the corresponding hydrocarbons; alkyl-phenols can be obtained from phenolic-aldehydes and -ketones; *p*-hydroxybenzophenone yields *p*-benzylphenol; benzoin and benzil yield dibenzyl; anthraquinone yields anthracene dihydride.

Esters can be reduced catalytically to hydrocarbons, see Am. Soc., 55, 1293.

x gms. of commercial granulated zinc are allowed to remain for about an hour at ordinary temperature in contact with about 2x c.cs. of a 5% aqueous solution of mercuric chloride. The supernatant liquid is poured off, and the ketone to be reduced together with hydrochloric acid (one

vol. conc. acid + two vols. water) added without previous washing or drying of the amalgam. The mixture is heated in a flask under a reflux condenser until a brisk evolution of hydrogen is noticed; and this is maintained at a steady rate by frequent addition of acid through the condenser. It is important that the two layers should be well mixed by the escaping gas. In the more tedious reductions large quantities of metal and acid are necessary to provide this agitation.

PREPARATION 104.—**Ethylresorcinol** (1-*Ethyl*-2 : 4-*dihydroxybenzene*).

$$C_2H_5C_6H_3(OH)_2. \qquad C_8H_{10}O_2. \qquad 138.$$

50 gms. of resacetophenone (p. 91) are treated as described above with 200 gms. of zinc amalgam and 600 c.cs. of 15% hydrochloric acid. When the reaction becomes vigorous, heating is stopped until it moderates. Heating is continued for about 3 hours with frequent additions of concentrated acid. The clear yellowish liquid is drained off from the zinc, saturated with common salt, extracted with ether, and the ethereal extract evaporated. The slightly yellowish liquid which remains soon solidifies, and may be crystallised easily from chloroform, giving a pure product,

$$CH_3CO.C_6H_3(OH)_2 \longrightarrow C_2H_5C_6H_3(OH)_2.$$

*Yield.*—Almost theoretical (44 gms.). Colourless crystals, soluble in cold water; M.P. 97°; sublimes on heating.

*n*-Hexylresorcinol, prepared from capronylresorcinol, is an important antiseptic. (E.P., 29,970 (1923).)

**Reaction LIX. Reduction of a Primary Aryl Hydrazine to the corresponding Hydrocarbon by the action of Copper Sulphate or Ferric Chloride.** (B., 18, 90, 786.) When a primary aryl hydrazine is boiled with neutral copper sulphate or ferric chloride, or treated with alkaline copper sulphate in the cold, the hydrazine radical is replaced by hydrogen, the corresponding aryl hydrocarbon being formed.

$$C_6H_5NH.NH_2 + 2CuO = C_6H_6 + N_2 + H_2O + Cu_2O.$$

This reaction can be employed to remove a primary amino group from an aromatic compound, especially when the ordinary method of direct reduction of the diazonium compound by sodium stannite or alcohol is not applicable. Although in the application of this method the hydrazine can be prepared as the hydrochloride, and reduced in the same solution, yet it is better to isolate the free base and oxidise it separately, since in the oxidation of the hydrochloride there is a tendency for the hydrazine radical to be replaced by chlorine.

**Reaction LX. Action of Water on Magnesium Alkyl or Aryl Halide** (Grignard). (B., 39, 634.)—When a Grignard compound is treated with water or other substance containing a hydroxyl group hydrolysis occurs, and the corresponding hydrocarbon is obtained.

$$C_6H_5.Mg.I + H_2O = C_6H_6 + OH.Mg.I.$$
$$C_6H_5MgI + C_2H_5OH = C_6H_6 + C_2H_5O.MgI.$$

This reaction is of theoretical rather than practical importance.

PREPARATION 105.—**Triphenylmethane.**

$HC(C_6H_5)_3$. $C_{19}H_{16}$. 244.

10 gms. (1 mol.) of triphenylmethyl chloride and 0·1 gms. of iodine are dissolved with gentle heating in 50 c.cs. of sodium-dried ether in a *dry* round-bottomed flask of 500 c.cs. capacity, fitted with a long reflux condenser, and 2 gms. (excess) of clean, dry magnesium filings or small pieces of the ribbon are added (see p. 73).

A slow stream of well-dried hydrogen is passed through the liquid by means of a tube through the cork to the bottom of the flask; the hydrogen coming from the top of the reflux condenser must be led to a good draught pipe, the flask being heated on a water bath to boiling, and the water bath removed. After the removal of the water bath the flask is wrapped in a cloth to conserve the heat of reaction, which is then sufficient to keep the ether boiling for about 1 hour, by which time bright yellow crystals of the magnesium compound separate. The mixture is again heated to boiling on a water bath for 1 hour, and then all the water is run out of the condenser. The ether evaporates and the solid magnesium compound remains. To it is added, after increasing the rate of passage of hydrogen with complete exclusion of air, 60 c.cs. (excess) of distilled water, and then, in small portions, 40 gms. of conc. sulphuric acid. The flask is well shaken and the contents boiled on a wire gauze for 15 minutes. The yellow crystalline cake of the magnesium compound at first floats on the surface, but gradually decomposes to a surface layer of homogeneous liquid. The reaction is complete when all the magnesium compound has disappeared and the whole is clear. Towards the end the flask is shaken vigorously at short intervals to prevent spurting of the accumulating oil. The flame is removed, the hydrogen stream shut off, and 150 c.cs. of pure benzene added to the liquid while still hot, the whole being vigorously shaken. The benzene solution, which is coloured red with iodine, is separated and treated in turn with warm water, warm aqueous caustic soda, warm sodium thiosulphate solution, and again with warm water. The turbid liquid is shaken with calcium chloride, and warmed until it becomes clear. It is filtered hot, allowed to stand over fresh calcium chloride for 24 hours, again filtered hot, and evaporated on a water bath to a bulk of 10 c.cs. On cooling, triphenylmethane crystals containing benzene of crystallisation separate. These crystals slowly lose benzene on standing and more quickly on heating on a water bath. The hydrocarbon is finally recrystallised from hot alcohol.

$$(C_6H_5)_3CCl \longrightarrow (C_6H_5)_3CMgCl \longrightarrow (C_6H_5)_3CH.$$

*Yield.*—90% theoretical (8 gms.). Colourless plates; soluble in benzene and in hot alcohol; M.P. 93°; B.P. 300°; separates from benzene in crystals containing 1 mol. of benzene of crystallisation; M.P. 76°. (B., 39, 634.)

**Reaction LXI. Reduction of Diazonium Compounds to the corresponding Hydrocarbon.** (A., 137, 39; B., 22, 587; 35, 162; 36, 815, 2065; 40,

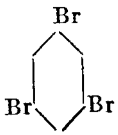
858.) When a diazonium compound is boiled with an alcohol, oxidation of the latter to the corresponding aldehyde and simultaneous replacement of the diazonium group by hydrogen occurs.

$$\begin{array}{l} R.\underset{\displaystyle Cl}{\underset{|}{N}} : N + C_2H_5OH \\ \qquad\qquad\qquad = RH + N_2 + HCl + CH_2CHO. \end{array}$$

This is the classical method of reducing diazonium compounds, but other reducing agents, notably sodium stannite, give better results; the alcohol always tends to form with the diazonium compound more or less of the corresponding mixed ether, unless a large number of negative groups be present. Hypophosphorous acid and alkaline sodium "hydrosulphite" also give good yields with certain types of compounds.

The method is much used to remove the amino group from an aromatic nucleus, and has had some important theoretical applications.

PREPARATION 106.—*s*-**Tribromobenzene** (1 : 3 : 5-*Tribromobenzene*).




$C_6H_3Br_3$. **315.**

50 gms. (1 mol.) of finely powdered *s*-tribromoaniline (O. S., XIII., 96) are treated with 300 c.cs. of absolute alcohol and 75 c.cs. of benzene added to insure complete solution. 20 c.cs. (excess) of conc. sulphuric acid are run in; should a precipitate form, it is redissolved by the addition of more benzene. 20 gms. (excess) of pure finely powdered sodium nitrite are added to the hot liquid as rapidly as possible without the reaction becoming too violent, and the whole heated until effervescence ceases. After standing over-night the precipitate is filtered, washed at the pump with hot water until the washings give no precipitate with barium chloride, dried on a porous plate and recrystallised from absolute alcohol.

$$C_6H_2Br_3NH_2 \xrightarrow[H_2SO_4]{NaNO_2} C_6H_2Br_3.N_2.SO_4 \xrightarrow{C_2H_5OH} C_6H_3Br_3.$$

*Yield.*—Almost theoretical (47 gms.). Colourless prisms; insoluble in water; M.P., 119°. (B., 22, 587; O. S., XIII., 96.)

PREPARATION 107.—**Diphenyl** (*Phenylbenzene*).

$C_6H_5.C_6H_5$. $C_{12}H_{10}$. **154.**

30 gms. (1 mol.) of benzidine are added to 60 c.cs. conc. hydrochloric acid and 400 c.cs. water. The whole is heated until the benzidine is dissolved. After cooling it is diazotised with 23 gms. (2 mols.) of sodium nitrite (see p. 380). To the ice-cold tetrazonium solution are added 350 c.cs. of commercial hypophosphorous acid (D. 1·15). After standing for several days in an ice chest, until no more solid separates, the diphenyl is

filtered off, treated with dilute caustic soda solution and steam distilled. It is then recrystallised from absolute alcohol.

$$NH_2C_6H_4.C_6H_4NH_2 \rightarrow ClN_2C_6H_4.C_6H_4N_2Cl \rightarrow C_6H_5.C_6H_5.$$

*Yield.*—60% theoretical (15 gms.). Colourless leaflets; insoluble in cold alcohol; M.P. 71°; B.P. 254°. (B., 35, 162.)

Hypophosphorous acid may be prepared by digesting 150 gms. finely powdered calcium hypophosphite with 45 c.cs. of conc. sulphuric acid, and 500 c.cs. water for 1 hour at 80°, and removing the calcium sulphate by filtration.

**Reaction LXII. Direct Reduction of Halogen Compounds.** (J. C. S., 45, 154; 47, 200.)—A very useful method for the preparation of hydrocarbons, more especially of aliphatic hydrocarbons, consists in replacing the halogen atom of a halogen compound by an atom of hydrogen.

$$RCl + H_2 = RH + HCl.$$

The reducing agents usually employed are phosphorus and hydriodic acid, or the zinc-copper or the aluminium-mercury couple. The couples have the advantage of readily yielding a pure gas, and are of wide application.

For the preparation of zinc-copper couples in alloy form, see O. S., XII., 87.

Methane can be prepared from methyl iodide or chloroform, etc., ethane from ethyl iodide, propane from propyl and isopropyl iodides, and so on.

The following will illustrate their use :—

PREPARATION 108.—**Methane.**

$$\begin{array}{c} H \\ | \\ H—C—H. \\ | \\ H \end{array} \qquad CH_4. \qquad 16.$$

To one limb of a wide U-tube cooled in water and filled with the zinc-copper, or the aluminium-mercury couple, is attached a small tap funnel, and to the other a small reflux condenser. The zinc-copper couple is prepared by placing 30 gms. (excess) of zinc in an aqueous solution of copper sulphate until the surface of the metal is covered with a film of metallic copper. The couple is washed with water and then with absolute alcohol. The aluminium-mercury couple, which gives a better yield of gas, is prepared by immersing 20 gms. (1 atom) of small pieces of sheet aluminium in mercuric chloride solution until a film of mercury covers the surface of the aluminium, which is washed as above. 100 c.c. (excess) of methyl alcohol (acidified with 2 drops of dilute sulphuric acid if the zinc-copper couple be used) are poured on to the couple in the U-tube and 50 gms. of methyl iodide are added gradually from the funnel so that the reaction does not become too violent nor the couple too hot. With the aluminium-mercury couple the reaction is especially vigorous, and good cooling is required. The gas is washed in worms containing (1) dis-

tilled water; (2) sodium methoxide dissolved in methyl alcohol—2 worms; (3) distilled water; (4) fuming sulphuric acid—2 worms; (5) conc. sulphuric acid—2 worms; (6) distilled water; (7) 50% caustic soda solution—2 worms. Conc. sulphuric acid is used to condense the acid mist from the fuming sulphuric acid washings; distilled water is always inserted between worms containing liquids, which will react violently if mixed. The gas is then passed through a U-tube heated in boiling water and containing palladium black to absorb hydrogen, of which usually about 1% is present. Alternatively, palladium oxide may be used in the tube to oxidise the hydrogen. The gas is collected in a gas-holder over 50% aqueous glycerol, which does not dissolve methane, under a slight excess pressure, as described in Preparation 99. If the dry gas be required, it is collected over mercury or conc. sulphuric acid, being first dried by passage through two U-tubes containing phosphorus pentoxide. To free it completely from hydrogen three or four treatments with palladium or its oxide will be necessary. The gas obtained in this way is pure provided care be taken that all air has been swept out of the apparatus before collection is begun. With proper precautions, the ratio-contraction on explosion to absorption by baryta water after explosion should always be between 1·99 and 2·01, the theoretical value being 2·00.

$$CH_3I + Zn + CH_3OH = ZnI(OCH_3) + CH_4.$$
$$3CH_3I + 2Al + 3CH_3OH = 3CH_4 + Al_2I_3(OCH_3)_3.$$

Colourless odourless gas; solubility in water at N.T.P. = 5·25; B.P. $^{760}$ − 164°; M.P. − 184°; explosive limits: in oxygen, 5—60%, in air, 6—13%. (J. C. S., 81, 541.)

## Purification by Fractional Liquefaction or Evaporation

If liquid air is available, the hydrogen in the methane prepared above is best removed by fractional distillation. The following is an outline of the method (see Fig. 52):—

The gas from the holder A is passed through a series of U-tubes containing phosphorus pentoxide, then through a small bulb B. When all the air has been driven out of the apparatus, a vacuum vessel containing liquid air is brought below B and gradually raised so as slowly to increase the cooled surface of the bulb. The methane condenses rapidly in B, hydrogen passing away through C. When A is almost empty of gas, the remainder is run away by means of the three-way tap D. Meanwhile the liquid air container is raised or lowered around B, so that the liquid in B gently boils. When about one-fifth has boiled away C is closed, and a small amount of gas allowed to pass away through D. Connection is then made to the gas-holder, which is slowly filled under a pressure slightly above atmospheric. If preferred, the methane may be distilled into another holder through C, and the gas from several holders, such as A, purified and collected in one holder. Great care must be taken in manipulating the liquid air container, so that the liquid in B boils gently; if the

vacuum vessel be lowered too rapidly, vigorous boiling will occur, and a great pressure generated in the apparatus. The last traces of gas in B are not collected.

This process can be repeated if a very pure gas is required. In each operation about one-third of the original gas is lost. The purity of the

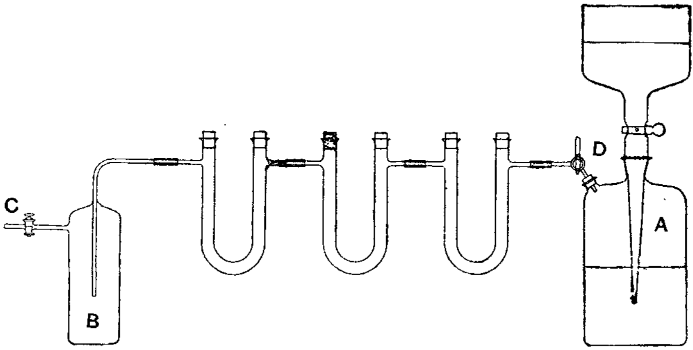



FIG. 52.

gas may be ascertained by inserting a platinum resistance thermometer in the liquefaction bulb, and determining the temperature during the operation, as in the fractional distillation of any other liquid. This is more important in preparing the higher hydrocarbons pure.

The methods of fractional liquefaction and distillation have very many similar and important applications in the chemistry of gases.

A convenient apparatus for delivering a gas at constant pressure is described in J. S. C. I., 47, 187.

# CHAPTER X

## HYDROGEN TO CARBON

## Hydroxy Compounds

### Alcohols and Phenols

THE reactions discussed below are based on the reduction of the group—

$$-\overset{|}{C}=O \quad \text{to} \quad -\overset{|}{C}H(OH).$$

Such reactions comprise practically all those in which hydrogen is linked to carbon to produce of necessity hydroxy compounds, which are of industrial importance, *e.g.*, the manufacture of methanol and higher alcohols from carbon monoxide and hydrogen in presence of catalysts, such as zinc-chromium oxides.

**Reaction LXIII. Combined Oxidation and Reduction of Aromatic Aldehydes under the influence of Caustic Alkalis** (Cannizzaro). (B., 14, 2394.)—The lower aliphatic aldehydes, except formaldehyde, are resinified by caustic alkali; aromatic aldehydes, however, and some of the higher aliphatic aldehydes behave differently, two molecules smoothly interacting to give, by simultaneous oxidation and reduction, one molecule each of the corresponding acid and alcohol.

$$R.CHO + R.CHO \longrightarrow RCH_2OH + R'COOH.$$

This method is frequently used for the preparation of aromatic alcohols from the corresponding aldehydes which can usually be readily obtained.

Salicylaldehyde does not undergo this reaction.

PREPARATION 109.—**Benzyl Alcohol** [*Phenyl-methanol*].

$$C_6H_5CH_2OH. \qquad C_7H_8O. \qquad 108.$$

and **Benzoic Acid** [*Phenylmethan acid*].

$$C_6H_5COOH. \qquad C_7H_6O_2. \qquad 122.$$

30 gms. (2 mols.) of freshly distilled benzaldehyde are mechanically shaken in the cold with 45 gms. (excess) of a 60% solution of caustic potash until a permanent emulsion is formed. The mixture is allowed to stand for 24 hours, during which time much potassium benzoate separates. Owing to the presence of conc. alkali, a glass stopper must not be used to close the shaking bottle. Water is added until a clear solution is obtained, which is then extracted four times with ether. The extract which contains the benzyl alcohol formed is shaken with conc. sodium bisulphite solution (see p. 504) to remove traces of benzaldehyde, washed

with dilute caustic soda and with water and filtered. The ether is removed on a water bath, and the residue fractionated, the fraction 204°—208° being redistilled to give pure benzyl alcohol.

The alkaline solution from which benzyl alcohol has been extracted is carefully neutralised, and acidified with, at first, concentrated, and then dilute hydrochloric acid. The precipitated benzoic acid is recrystallised from hot water.

$$2C_6H_5CHO + KOH = C_6H_5CH_2OH + C_6H_5COOK.$$

*Yield.*—90% theoretical of both compounds (benzyl alcohol, 13·5 gms.; benzoic acid, 15·5 gms.).

*Benzyl Alcohol.*—Colourless oil somewhat soluble in water; faintly aromatic odour; B.P. 206·5°; D. $^{15·4}_{4}$ 1·05.

*Benzoic Acid.*—Colourless needles; soluble in hot water, alcohol, ether; melts and sublimes on heating; can be distilled in steam; M.P. 122°; B.P. 250°. (B., 14, 2394.)

**Reaction LXIV.** (*a*) **Reduction of Aldehydes and Ketones to the corresponding Alcohols by the use of Alkaline Reducing Agents.** (B., 31, 1003; J. pr., [2], 33, 184; [2], 76, 137.)—The alkaline reducing agent most usually employed is sodium amalgam and water, especially to obtain polyhydric alcohols from the corresponding sugars; here it is easily applied owing to the solubility of the sugars in water. But even if the ketone or aldehyde be not soluble in water, the amalgam can be allowed directly to act on the moist substance, or the latter can be dissolved in ether or benzene, and the amalgam and water gradually added. Aluminium amalgam or ethylate can be employed (O. S., XV., 84). Sodium and alcohol (see also Reaction CLXXIV.) are generally used in the aromatic series. In reducing ketones, especially aliphatic ketones, there is always more or less pinacone formation; this is not so marked in the aromatic series, especially if acid reducing agents are not used (p. 54). Here zinc dust and caustic soda or ammonia, and alcoholic sodium "hydrosulphite" give good results. The Sabatier-Senderens reaction can also be employed (see p. 172).

PREPARATION 110.—**Dulcitol** (*Hexahydroxyhexane* + — — +).

$$CH_2OH.(CHOH)_4CH_2OH. \qquad C_6H_{14}O_6. \qquad 182.$$

10 gms. (1 mol.) of galactose dissolved in 100 gms. of water are shaken in a stout 500-c.c. stoppered bottle with 300 gms. of $2\frac{1}{2}$% sodium amalgam (see p. 508) until the first reaction has ceased. Every 10 minutes the liquid is neutralised with 10% sulphuric acid. Further amalgam is added in 20-gm. lots with shaking and neutralisation as before, until 1 c.c. of the solution reduces no more than 0·2 c.c. of Fehling's solution (p. 499).

The temperature throughout must not exceed 20°; the operation takes about 3 hours, and 400 gms. (excess) of $2\frac{1}{2}$% amalgam are required. When reduction is complete, the solution is separated from the mercury, exactly neutralised with 10% sulphuric acid, heated on a water bath to

60°, and poured with stirring into 1 litre of alcohol, and the precipitated sodium sulphate filtered off at the pump. The filtrate is concentrated on a water bath to about 25 c.cs., and until crystals begin to separate, the alcohol being recovered. The residual liquid is cooled to 0° and filtered. The precipitated sodium sulphate is extracted with 80% alcohol to recover any dulcitol it may contain.

$$CH_2OH.(CHOH)_4.CHO \xrightarrow{H_2} CH_2OH.(CHOH)_4CH_2OH.$$

*Yield.*—50% theoretical (5 gms.). Colourless crystals; sweet taste; very soluble in water; M.P. 188°. (B., 20, 1091; 25, 2564.)

PREPARATION 111.—**Phenylmethylcarbinol** [1-*Phenyl*-1-*ethanol*].

$CH(CH_3)(C_6H_5)(OH)$. $C_3H_{10}O$. 122.

15 gms. (1 mol.) of acetophenone are dissolved in 150 gms. of absolute alcohol, and the whole warmed on a water bath. 15 gms. (excess) of sodium wire are rapidly added, and when reaction has ceased, carbon dioxide is passed in until it is no longer absorbed. 350 c.cs. of water are added and the mixture evaporated on a water bath until nothing further distils, the alcohol being recovered. The residue is extracted with ether and dried over potassium carbonate, the ether removed on a water bath, and the residue fractionated under reduced pressure, the fraction 97°—103° at 15 mm. being retained. (*Cf.* Preparation 19.)

$$C_6H_5CO.CH_3 \xrightarrow{H_2} C_6H_5.CHOH.CH_3.$$

*Yield.*—45% theoretical (6·5 gms.). Colourless liquid; slightly soluble in water; B.P.$^{760}$, 198°; B.P.$^{40}$, 118°; B.P.$^{20}$, 111°; B.P.$^{15}$, 100°. (B., 31, 1003.)

PREPARATION 112.—**Benzhydrol** [*Diphenyl-methanol*].

$HC(C_6H_5)_2(OH)$. $C_{13}H_{12}O$. 184.

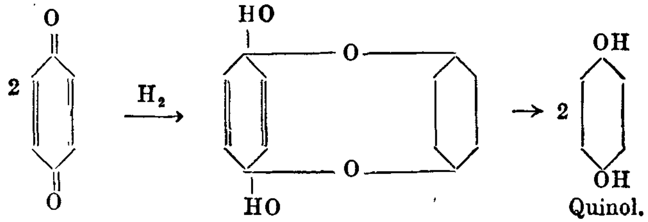
10 gms. (1 mol.) of benzophenone are dissolved in 200 c.cs. of alcohol, and 40 gms. of 50% aqueous caustic potash added, and the mixture boiled until it turns dark brown. The mixture is treated gradually with 100 gms. of zinc dust until the brown colour disappears. The hot solution is filtered, and the filtrate poured into ice-water acidified with hydrochloric acid. Benzhydrol separates and may be crystallised from alcohol.

$$(C_6H_5)_2CO \xrightarrow{H_2} (C_6H_5)_2CHOH.$$

*Yield.*—90% theoretical (9 gms.). Colourless needles; slightly soluble in water; M.P. 68°. (J. pr., [2], 33, 184; O. S., VIII., 24.)

**Reaction LXIV.** (*b*) **Reduction of Quinones.** (A., 27, 268; 45, 354; 215, 127; B., 19, 1467; 20, 1854, 2283; 21, 1172; 40, 390, 924; J. pr., [2], 76, 141; Meyer and Jacobson, Lehrbuch (ii.) 421.)—All benzoquinones are very readily reduced to the corresponding quinols, sulphurous acid

being the reagent most usually employed. In the reduction the greenish coloured quinhydrone (see p. 224) is intermediately formed.



Benzoquinone. Quinhydrone. Quinol.

Phenylhydrazine and hydroxylamine also reduce quinone to quinol; they do not react with it as with other carbonyl compounds.

The anthraquinones may be reduced to the corresponding "anthraquinols" (hydroxyanthranols) with alkaline sodium "hydrosulphite"; this reaction has a wide application in the dye industry. These compounds are difficult to isolate pure, for they rapidly oxidise in air. The anthranols —$\gamma$-monohydroxyanthracenes—however, are stable, and may be obtained by reducing anthraquinone with acid-reducing agents—tin and hydrochloric acid, zinc and glacial acetic acid, copper or aluminium, and sulphuric acid, etc. For the complete reduction of anthraquinone, see Reaction LVIII. (*a*).

PREPARATION 113.—**Quinol** (1 : 4-*Dihydroxybenzene*).

$$C_6H_4(OH)_2[1:4]. \qquad C_6H_6O_2. \qquad 110.$$

10 gms. of finely powdered quinone are suspended in cold water, and the liquid saturated with sulphur dioxide until, after the intermediate formation of quinhydrone, complete solution and decolorisation have occurred, the operation being carried out in a fume cupboard. The liquid is repeatedly extracted with ether until nothing further is removed, the ether expelled on a water bath, and the residue recrystallised from dilute sulphurous acid with the addition of animal charcoal.

If preferred, the crude suspension of quinone obtained from 25 gms. of aniline (see p. 235) may be employed, being saturated with sulphur dioxide until it smells very strongly of the gas. After standing for 2 hours, if it still smells of the gas the liquid is extracted with ether, as above. If the odour of the gas has vanished, the liquid must be resaturated, and so on, until the smell persists for 2 hours.

$$C_6H_4O_2 \xrightarrow{H_2} C_6H_4(OH)_2.$$

*Yield.*—80% theoretical (8 gms.). Colourless prisms; soluble in ether, alcohol, and warm water; sublimes at a gentle heat; M.P. 169°. (A., 27, 268; 45, 354; 215, 127; B., 19, 1467; 20, 2283.)

PREPARATION 114.—**Anthranol** ($\gamma$-*Hydroxyanthracene*).

$$C_6H_4\left\langle\begin{array}{c}CH\\|\\COH\end{array}\right\rangle C_6H_4. \qquad C_{14}H_{10}O. \qquad 194.$$

10 gms. (1 mol.) of anthraquinone and 30 gms. (excess) of granulated zinc are refluxed with 500 c.cs. of glacial acetic acid, the operation being performed in a good fume cupboard. Conc. hydrochloric acid, a few c.cs. at a time, is added until no coloration occurs, and hydrogen is continuously evolved. After $\frac{1}{4}$ hour and when a sample no longer deposits crystals on cooling, the whole is cooled, poured into dilute hydrochloric acid, and the precipitate recrystallised from glacial acetic acid, to which a little zinc dust and hydrochloric acid have been added to prevent reoxidation.

*Yield.*—80% theoretical (14·5 gms.). Colourless needles; insoluble in water; M.P. (decomposition) 170°. (B., 20, 1854; D.R.P., 201542.)

**Reaction LXIV.** (*c*) **Catalytic Hydrogenation of Acids and Esters to the Corresponding Alcohols.** (Z. a., 44, 714; Am. Soc., 53, 1095; B., 64, 2051.)—Various catalysts are used, *e.g.*, copper chromite, nickel, at temperatures of 250°—300°, and usually high pressures (200 atm.). Temperatures of 350° and over result in hydrocarbon formation.

$$\underset{\text{Ethyl oleate.}}{CH_3(CH_2)_7CH : CH(CH_2)_7COOC_2H_5} \longrightarrow \underset{\text{Octadecyl alcohol.}}{CH_3(CH_2)_{16}CH_2OH.}$$

Under certain conditions hydrogenation may be confined to the —COOH group, *e.g.*, oleic acid $\longrightarrow$ oleyl alcohol.

Salts of the hydrogen sulphate esters of these higher alcohols are used extensively in the textile industries, those of the unsaturated alcohols possessing superior properties in certain respects.

The reaction is widely applied to the production of higher alcohols from oils and fats.

# CHAPTER XI

## HYDROGEN TO CARBON

## Oxy and Hydroxy-oxy Compounds

### Aldehydes, Ketones and Acids

The reductions in this section are mostly those of acids to aldehydes; they are naturally few, since oxygenated compounds are not usually obtained by reduction of more highly oxygenated substances; the reverse process is much more often employed.

**Reaction LXV.** (*a*) **Reduction of Phenolic Acids to the corresponding Aldehydes by the action of Sodium Amalgam and Boric Acid in the presence of a Primary Aromatic Amine.** (B., 41, 4147.)—This is one of the few methods of reducing an acid to the corresponding aldehyde in satisfactory yield. The presence of the primary aromatic base is essential to protect the aldehyde; it condenses with it as formed, and inhibits further reduction to the alcohol. A weak acid such as boric acid is used partly because salt formation by the base would hinder condensation and partly to avoid hydrolysis of the condensation product.

$$OH.C_6H_4.COOH \xrightarrow{H_2(R_1NH_2)} OH.C_6H_4.CH:NR_1 \xrightarrow{H_2O} OH.C_6H_4.CHO.$$

This method of preparing phenolic aldehydes has the advantage over Reimer's (pp. 104, 123) of not giving a mixture of isomers. The yields also are improved.

Preparation 115.—**Salicylaldehyde** (*o-Hydroxybenzaldehyde*).

$C_6H_4(OH)(CHO)[1:2]$. $C_7H_6O_2$. 122.

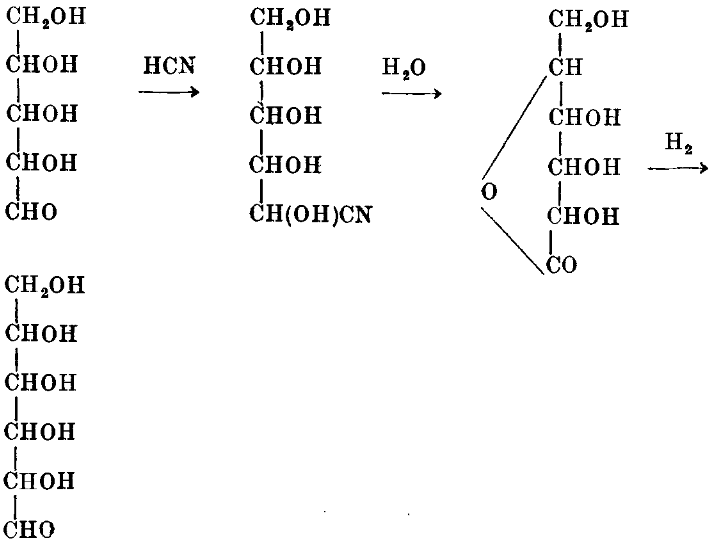
20 gms. (1 mol.) of salicylic acid dissolved in hot water are neutralised with N/1 caustic soda, using phenolphthalein as indicator, and the solution diluted to 1 litre and boiled. 30 gms. (excess) of *p*-toluidine are added, and the whole cooled and mechanically stirred. 400 gms. of sodium chloride and 30 gms. (excess) of boric acid are added gradually, and still with stirring 400 gms. (excess) of $2\frac{1}{2}\%$ sodium amalgam (see p. 508), the solution being maintained faintly acid by the addition of boric acid (about 200 gms.) from time to time. The reaction is complete when a sample, after filtration and acidification with hydrochloric acid, gives no precipitate of salicylic acid. The condensation product of the aldehyde and base is filtered at the pump, suspended in 10% sulphuric acid, and distilled in steam. The aldehyde distils and is extracted from the distillate with ether. The extract is dried over calcium chloride, the ether removed on a water bath, and the residue fractionated between 195° and

197°. The aldehyde may also be purified by means of its bisulphite compound (see Preparation 156).

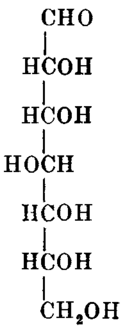
$$C_6H_4(OH)(COOH) + H_2 + (CH_3)(C_6H_4)NH_2$$
$$\rightarrow C_6H_4(OH)CH : NC_6H_4CH_3 + 2H_2O$$
$$\rightarrow C_6H_4(OH)CHO + H_2N.C_6H_4.CH_3.$$

*Yield.*—60% theoretical (8 gms.). Colourless crystals or liquid; pungent odour; soluble in water; miscible in all proportions with alcohol and ether; volatile in steam; M.P. 20°; B.P. 196·5°; D. $^{13·5}_{4}$, 1·173. (B., 41, 4147.)

**Reaction LXV.** (*b*) **Reduction of Lactones to the corresponding Hydroxy-aldehydes by the action of Sodium Amalgam in faintly Acid Solution.** (A., 270, 72, 87; 272, 200.)—This is a reaction very similar to the previous one. It finds an extensive application in the sugar group for reducing the lactones of the poly-hydroxy acids to the corresponding aldoses. Combined with the cyanohydrin reaction (see p. 155) it forms a means of passing from one group of sugars to the next higher group—thus:

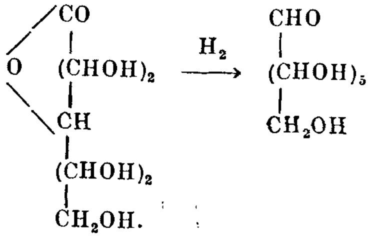



PREPARATION 116.—α-**Glucoheptose** (*Hexahydroxy-heptanal* + + — + +).




$C_7H_{14}O_7$. 210.

15 gms. (1 mol.) of the lactone of α-glucoheptonic acid (see p. 128) are dissolved in 150 c.cs. of water in a thick-walled 500-c.c. vessel, and are cooled in a freezing mixture to 0°. 2 c.cs. of 10% sulphuric acid are added, and the whole mechanically agitated, being meanwhile kept immersed in the freezing mixture. 125 gms. (excess) of $2\frac{1}{2}$% sodium amalgam (see p. 508) are added, and at intervals further 2-c.c. lots of 10% sulphuric acid, so that the liquid always remains acid. The temperature must not be allowed to rise above 5°. In about 10 minutes the amalgam is used up, a further 125 gms. are added, and the procedure of treating with acid repeated. The whole operation takes about 40 minutes. The solution is separated from the mercury and any unchanged lactone, and converted to the sodium salt by adding sodium hydroxide until the liquid remains alkaline after standing for 30 minutes. The solution is then exactly neutralised, at first with 5% and ultimately with N/1 sulphuric acid, brought to the boil with animal charcoal and filtered; 8 volumes of hot alcohol are added with constant stirring, the whole left at room temperature for 12 hours, and sodium sulphate and most of the organic sodium salts present which are precipitated are filtered off at the pump. The filtrate is slowly concentrated until crystallisation begins, is cooled and after some hours filtered at the pump. The precipitate is washed first with 55% then with 85%, and finally with absolute alcohol.




*Yield.*—35% theoretical (5 gms.). Colourless crystals; soluble in water; M.P. 190° (M.P. osazone 195°). (A., 270, 72, 87; 272, 200.)

**Reaction LXVI.** (*a*) **Reduction of Unsaturated Acids by means of Sodium Amalgam in Alkaline Solution.** (A., 121, 375; 137, 237.)—The preparation below illustrates an important application of sodium amalgam, this substance being especially useful for reducing groups or double bonds in compounds containing carboxyl, as the alkali present keeps the substance in solution and protects the acid group.

PREPARATION 117.—**Hydrocinnamic Acid** [3-*Phenylpropan acid*].

$$C_6H_5.CH_2.CH_2.COOH. \qquad C_9H_{10}O_2. \qquad 150.$$

20 gms. (1 mol.) of cinnamic acid dissolved in a little more than the equivalent amount of caustic soda (145 c.cs. of N-solution) are placed in a stout-walled vessel fitted with a mechanical stirrer and 350 gms. (excess) of $2\frac{1}{2}$% sodium amalgam (see p. 508) are added gradually with vigorous agitation in the course of 1 hour. When no more hydrogen is evolved, the mercury is separated, washed with water, the washings being added

to the rest. The liquid is acidified with an excess of 20% hydrochloric acid; on cooling an oil separates, which, on rubbing with a glass rod, solidifies; it is filtered off at the pump, dried, and recrystallised from petroleum ether, or from *warm* water, crystallisation at a low temperature being necessary owing to the relatively low melting point of the substance.

$$C_6H_5.CH : CH.COOH + H_2 = C_6H_5.CH_2.CH_2.COOH.$$

*Yield.*—85% theoretical (17 gms.). Colourless prisms; insoluble in cold, somewhat soluble in warm water; soluble in alcohol; volatile in steam. M.P. 47°; B.P. 280°. (A., 121, 375; 137, 237.)

**Reaction LXVI.** (*b*) **Reduction of Hydroxy-Acids by the action of Hydriodic Acid.** (A., 114, 106.)—Hydriodic acid is especially useful in reducing groups or ethylene linkages in acids as, although a powerful reducing agent, it does not readily attack the carboxyl group. It may be used either in a solvent, *e.g.*, glacial acetic acid, or more usually the reaction is carried out by heating to a high temperature in a sealed tube. Red phosphorus is usually added to convert the liberated iodine into hydriodic acid; thus a small amount of hydriodic acid can reduce a large quantity of substance.

$$R_1R_2C(OH)COOH + 2HI = R_1R_2CHCOOH + H_2O + I_2.$$

For the conversion of maleic to succinic acid (*a*) by reduction with hydriodic acid, see U. S. P., 1,914,870, and (*b*) by reduction with hydrogen and nickel, see U. S. P., 1,491,465.

PREPARATION 118.—**Succinic Acid** [*Butan di-acid*].

$$COOH.CH_2.CH_2.COOH. \qquad C_4H_6O_4. \qquad 118.$$

10 gms. (1 mol.) of malic acid are dissolved in 40 gms. (excess) of 57% (constant boiling mixture) hydriodic acid (see p. 506) and the solution, together with 3 gms. of red phosphorus, heated in a sealed tube (see p. 41) in a tube furnace at 130° for 6 hours. When cool, the tube is opened (*caution!* see p. 44), the contents evaporated to dryness on a water bath, and the cold residue extracted with small quantities of chloroform until no more free iodine is removed. The succinic acid is then heated at 70° to remove all traces of chloroform, and recrystallised from hot water.

$$COOH.CHOHCH_2.COOH + 2HI = COOH.CH_2.CH_2.COOH + H_2O + I_2.$$

*Yield.*—60% theoretical (5 gms.). Colourless prisms; soluble in water, alcohol and ether; insoluble in chloroform; M.P. 182°. (A., 114, 106.)

PREPARATION 119.—**Diphenylacetic Acid** [*Diphenylethan acid*].

$$(C_6H_5)_2CH.COOH. \qquad C_{14}H_{12}O_2. \qquad 212.$$

20 gms. (1 mol.) of benzilic acid (see p. 111), 10 gms. of 57% hydriodic acid (constant boiling acid), 10 gms. of red phosphorus (excess of P + HI) and 120 gms. of glacial acetic acid are refluxed in a round-bottomed flask, in a fume chamber for 2 hours. The solution is filtered at the pump,

poured while still hot into an excess of water, the precipitate filtered off at the pump, washed with water and recrystallised from alcohol.

$$(C_6H_5)_2C(OH)COOH + 2HI = (C_6H_5)_2CHCOOH + H_2O + I_2.$$

*Yield.*—80% theoretical (14 gms.). Colourless crystals; insoluble in cold alcohol; M.P. 146°. (A., 275, 84; O. S., III., 45.)

**Reaction LXVII.** (*a*) **Ketonic Hydrolysis of Alkyl Derivatives of Ethyl Acetoacetate.** (A., 138, 211.)—This reaction illustrates one of many synthetical uses of acetoacetic ester. When that ester or its mono- or di-alkyl derivatives is boiled with *dilute* aqueous or alcoholic alkalis or baryta water, or sulphuric acid, "ketonic hydrolysis" occurs, and acetone or its mono- or di-substituted derivatives is formed—

$$\begin{array}{rcc}CH_3COCR_1R_{11} & CO & OC_2H_5 \\ H & O & H\end{array}$$

$$\longrightarrow CH_3CO.CHR_1R_{11} + CO_2 + C_2H_5OH.$$

Compounds such as aceto-succinic ester and its derivatives which contain the acetoacetic ester grouping also undergo this hydrolysis.

$$\begin{array}{l}\quad H—OH \\ CH_3CO.CH.COOC_2H_5 \\ \qquad | \\ CH_3CO.CH.COOC_2H_2 \\ \quad H—OH\end{array} \longrightarrow CH_3CO.CH_2CH_2.COCH_3 + 2CO_2 + 2C_2H_5OH.$$

PREPARATION 120.—**Methyl Ethyl Ketone** [*Butanon*].

$$CH_3.CO.C_2H_5. \qquad C_4H_8O. \qquad 72.$$

20 gms. (1 mol.) of methylacetoacetic ester are refluxed with 250 c.cs. of saturated baryta water until the oily layer disappears. The solution is then distilled on a water bath to 90°. The distillate is mechanically shaken for 3 hours with a freshly prepared saturated solution of sodium bisulphite, and the crystals collected and distilled with an excess of dilute sulphuric acid or sodium carbonate solution at 90°. The distillate is dried over calcium chloride and redistilled, the fraction 79°—82° being retained.

$$CH_3COCH(CH_3)COOC_2H_5 + H_2O = CH_3.COCH_2CH_3 + CO_2 + C_2H_5OH.$$

*Yield.*—70% theoretical (7 gms.). Colourless mobile liquid; pleasant odour; miscible with water; B.P. 81°. (A., 138, 211.)

In an exactly similar way acetone (B.P. 56°) can be prepared from acetoacetic ester (see p. 148); methyl propyl ketone (B.P. 102°) from monoethyl acetoacetic ester (see p. 140). The higher ketones may be purified by washing with saturated brine until alcohol is removed; they are then, after drying over calcium chloride, fractionated. In all these hydrolyses dilute aqueous or alcoholic potash, or dilute sulphuric acid, may be used in place of baryta water. The yields in these preparations are all of the same order—70%.

PREPARATION 121.—**Acetonylacetone** [2 : 5-*Hexandion*].

$CH_3COCH_2.CH_2.COCH_3$. $C_6H_{10}O_2$. 114.

20 gms. (1 mol.) of di-aceto-succinic ester (see p. 150) are mechanically shaken for several days with 250 c.cs. (excess) of 5% aqueous caustic soda, and until no di-aceto-succinic ester separates on acidification of a sample with dilute hydrochloric acid. The solution is then saturated with potassium carbonate and extracted with ether, the extract is washed with brine to remove alcohol, dried over calcium chloride, and distilled, the fraction 192°—198° being retained.

$$\begin{array}{l} CH_3COCH.COOC_2H_5 \\ \quad\quad\;\;| \\ CH_3COCH.COOC_2H_5 \end{array} + 2H_2O =$$
$$CH_3COCH_2.CH_2COCH_3 + 2CO_2 + 2C_2H_5OH.$$

*Yield.*—70% theoretical (6 gms.). Colourless liquid; agreeable odour; miscible with water, alcohol and ether; M.P. − 9°; B.P. 194°; D. $^{20}_{4}$ 0·973. (B., 18, 58; 33, 1217.)

**Reaction LXVII.** (*b*) **Acid Hydrolysis of Alkyl Derivatives of Ethyl Acetoacetate.** (B., 19, 227.)—When acetoacetic ester or its mono- or di-alkyl derivatives are refluxed with *concentrated* aqueous or alcoholic potash, acid hydrolysis occurs and 2 mols. of acetic acid, or 1 mol. of that acid, and 1 mol. of a mono- or di-substituted derivative are obtained.

$$\begin{array}{l} CH_3CO-CR_1R_{11}COOC_2H_5 \\ \quad\;\; HO-H \end{array} \rightarrow CH_3COOH + HCR_1R_{11}COOH.$$

It is not possible to perform the acid hydrolysis without some ketonic hydrolysis occurring. This reaction and the preceding one are important in many syntheses of aliphatic ketones and acids. They might have been included equally well in the decomposition section (p. 411); in fact they are often referred to as the "ketonic" and "acid" decomposition of acetoacetic ester. The malonic ester synthesis of fatty acids may be compared with the present reaction (p. 135).

PREPARATION 122.—**Methylethylacetic Acid** [2-*Methylbutan acid*].

$HC(CH_3)(C_2H_5)COOH$. $C_5H_{10}O_2$. 102.

20 gms. (1 mol.) of methyl ethyl acetoacetic ester are refluxed for 4 hours with 40 gms. (excess) of caustic potash dissolved in 15 gms. of 50% alcohol. The mixture is poured into 250 c.cs. of water and acidified after extraction with ether to remove unchanged ester and methyl-*iso*-butyl ketone, a by-product forms as in the previous reaction. The acid which separates as an oil is extracted with ether, the extract dried over calcium chloride, and distilled, the fraction 172°—178° being retained.

$$CH_3.CO.C(CH_3)(C_2H_5)COOC_2H_5 + 2H_2O$$
$$= CH_3.COOH + CH(CH_3)(C_2H_5)COOH + C_2H_5OH.$$

*Yield.*—60% theoretical (11 gms.). Colourless liquid; B.P. 175°. (B., 19, 227; O. S., V., 75.)

In an exactly similar way the esters shown in the following table yield the corresponding acids.

| Ester. | Corresponding Acid. | B.P. |
|---|---|---|
| Acetoacetic ester | Acetic acid | 119° |
| Methyl acetoacetic ester | Propionic acid | 141° |
| Ethyl acetoacetic ester | Butyric acid | 162° |
| Dimethyl acetoacetic ester | *Iso*butyric acid | 154° |
| Diethyl acetoacetic ester | *Iso*caproic acid | 190° |

The higher acids need not be extracted from the acidified reaction product with ether, but may be separated directly as they are only very slightly soluble in water.

# CHAPTER XII

## HYDROGEN TO CARBON

### HALOGEN COMPOUNDS

ONLY two reactions are of sufficient importance to be considered here.

**Reaction LXVIII. Simultaneous Reduction and Halogenation of Polyhydric Alcohols.** (A., 138, 364.)—When polyhydric alcohols are heated with hydriodic acid, reduction of all the hydroxyl groups save one occurs; this latter is replaced by iodine to form a secondary iodide. In this way, *e.g.*, dulcitol, or any of the hexose alcohols, yields normal secondary hexyl iodide; this is of importance in determining the chain structure of the sugars. This reaction probably occurs—

$$\begin{array}{c} CH_2OH \\ | \\ (CHOH)_4 \\ | \\ CH_2OH \end{array} \xrightarrow{HI} \begin{array}{c} CH_2I \\ | \\ (CHI)_4 \\ | \\ CH_2I. \end{array}$$

$$\xrightarrow{HI} \begin{array}{c} CH_3 \\ | \\ CHI \\ | \\ (CH_2)_3 \\ | \\ CH_3. \end{array}$$

The primary iodide is never formed in such reactions.

PREPARATION 123.—*iso*-**Propyl Iodide** [2-*Iodopropan*].

$$CH_3.CHICH_3. \qquad C_3H_7I. \qquad 170.$$

70 gms. (excess) of iodine, 45 gms. (excess) of glycerol, and 30 gms. (excess) of water are placed in a 250-c.c. retort connected with a condenser and receiver and placed in a fume chamber. 10 gms. (5 atoms) of yellow phosphorus (*caution !*) are added gradually in small pieces, the phosphorus being cut under water, and transferred to the retort with crucible tongs. The violent reaction which usually occurs on adding the phosphorus must be allowed to subside before any more is added. Should no reaction take place on adding the first three pieces of phosphorus, the retort is immersed in warm water until interaction commences. When the addition of the phosphorus is complete the retort is heated on a wire gauze until no further oily liquid distils. The distillate is replaced in the retort and redistilled, washed in turn with 10% caustic soda, with sodium thio-

sulphate, again with 10% caustic soda and with water; it is dried over calcium chloride for 24 hours and fractionated between 88°—90°.

$$5P + 15I = 5PI_3.$$
$$5PI_3 + 15H_2O = 15HI + 5P(OH)_3$$
$$\begin{array}{l} \quad CH_2OH \\ 5\ \dot{C}HOH \\ \quad \dot{C}H_2OH \end{array} + 15HI = \begin{array}{l} \quad CH_2I \\ 5\ \dot{C}HI \\ \quad \dot{C}H_2I \end{array} + 15H_2O.$$
$$\begin{array}{l} \quad CH_2I \\ \quad\ | \\ 5\ CHI \\ \quad\ | \\ \quad CH_2I \end{array} + 10HI = \begin{array}{l} \quad CH_3 \\ \quad\ | \\ 5\ CHI \\ \quad\ | \\ \quad CH_3 \end{array} + 10I_2.$$

1 : 2 : 3-Triiodopropane is probably formed as an intermediate compound, but it is as yet unknown in the free state.

*Yield.*—80% theoretical (70 gms.). Colourless liquid; insoluble in water; B.P. 89°; D. $^{0}_{4}$ 1·744. (A., 138, 364.)

**Reaction LXIX. Partial Reduction of Trihalogen to Dihalogen Compounds.** (C. r., 145, 810; 146, 1282; B., 52, 212.)—By a suitable choice of the reaction conditions halogen compounds, containing three halogen atoms linked to one carbon atom, may be reduced to dihalogen compounds. This is an important method of preparing the latter pure; it is not easy to obtain them by direct halogenation owing to the difficulty of controlling the reaction. The success of the reduction depends on the reagent used; sodium arsenite, for instance, reduces iodoform to methylene iodide in 95% yield. A somewhat similar reaction is seen in the simultaneous reduction and oxidation of chloral hydrate to dichloroacetic acid by the action of potassium cyanide or ferrocyanide.

$$CCl_3.CH(OH)_2 + KCN = CHCl_2.COOH + HCN + KCl.$$

PREPARATION 124.—**Methylene Iodide** (*Diiodomethane*).

$$\begin{array}{c} H \\ | \\ I—C—H. \\ | \\ I \end{array} \qquad CH_2I_2. \qquad 268.$$

100 gms. (1 mol.) of iodoform are placed in a round-bottomed flask fitted with a mechanical agitator, a reflux condenser, a dropping funnel, and a thermometer. 50 c.cs. of sodium arsenite solution prepared from 27·5 gms. of arsenious oxide (excess), 53 gms. caustic soda (excess) and 260 c.cs. of water are then added. Agitation is started and the temperature is raised to 60°—65°. The remainder of the arsenite solution is now gradually added during about 30 minutes, and the whole allowed to stand for a further hour, the temperature being maintained at 60°—65° throughout. The mixture is cooled to 40°, and filtered to remove mechanical impurities; the filtrate consists of an aqueous solution with a pale yellow oil underneath. The oil is separated, dried over calcium chloride for

24 hours, and distilled under reduced pressure, the fraction 106°—107° at 70 mms. being retained.

$$CHI_3 + Na_3AsO_3 + NaOH = CH_2I_2 + NaI + Na_3AsO_4.$$

*Yield.*—95% theoretical (65 gms.). Colourless oil ; insoluble in water ; B.P. 181° (with decomposition) ; D. $^{15}_{15}$, 3·3326 ; (C. r., 145, 810 ; 146, 1282 ; B., 52, 212 ; O. S., I., 57).

# CHAPTER XIII

## THE LINKING OF OXYGEN TO CARBON

## HYDROXY COMPOUNDS

### Alcohols and Phenols

THIS section comprises a great number of reactions since, besides those which may be classed under the heading of oxidations—and such reactions alone form a large branch of practical organic chemistry—it also includes " hydroxylation reactions," which also are numerous. Below is given a selection of the more important, but it will be understood that many more reactions would have to be included before anything approaching completion would be attained. They indicate for the most part methods of replacing various elements and groups, attached to carbon, by the hydroxyl (OH) group.

**Reaction LXX. Oxidation of certain Hydrocarbons.** (B., 14, 1944 ; A. Spl., 1869, 300 ; E.P., 1948 (1869).)—This reaction is confined in the aliphatic series almost exclusively to the replacement by hydroxyl of the hydrogen attached to tertiary carbon atoms. A powerful oxidising agent, *e.g.*, chromic acid in glacial acetic acid, is necessary. In the aromatic series the reaction is somewhat more easy to accomplish ; when the sodium salt of anthraquinone-$\beta$-monosulphonic acid, for example, is fused under pressure with caustic soda and a little potassium chlorate, replacement of both a hydrogen atom and the sulphonic acid group by hydroxyl occurs, and alizarin ($\alpha\,\beta$-dihydroxyanthraquinone) is obtained.

$$C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle C_6H_3SO_3Na(\beta) \xrightarrow[O]{NaOH} C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle C_6H_2(OH)_2[\alpha\ \beta].$$

Alizarin.

PREPARATION 125.—**Triphenylcarbinol** [*Triphenyl-methanol*].

$(C_6H_5)_3C(OH)$. $C_{19}H_{16}O$. 260.

12 gms. (1 mol.) of triphenylmethane dissolved in 60 gms. of glacial acetic acid are treated gradually in the warm with 12 gms. (excess) of chromic acid. Gentle heating is continued until a sample poured into water gives a precipitate which does not melt below 100° (1—2 hours). The whole is then poured into water and the precipitate filtered, washed with water, dried on a water bath, and recrystallised from benzene.

$$(C_6H_5)_3CH + O = (C_6H_5)_3C(OH).$$

*Yield.*—85% theoretical (11 gms.). Colourless crystals ; soluble in hot benzene and glacial acetic acid ; M.P. 158°. (B., 14, 1944.)

**Reaction LXXI. Replacement of Halogen by Hydroxyl.** (B., 14, 2394; 16, 2954; 25, 3290; J. pr., 11, 229; A. Ch., [3], 55, 400.)—When alkyl halides are refluxed with dilute caustic alkali or alkali carbonate, hydroxylation occurs smoothly. If the halide be tertiary the replacement takes place with great ease, warming with water being sufficient; a secondary halide reacts less readily, but more so than a primary. Halogen in aromatic compounds is replaced with great difficulty unless there be present negative substituents in the *ortho-* or *para*-position. The replacement, however, can be effected under pressure (U.S.P., 1996745).

$$C_6H_3Cl(NO_2)_2 \longrightarrow C_6H_3(OH)(NO_2)_2.$$

Steam can be used to bring about the hydroxylation if the heating is carried out under pressure. (E.P., 358903.)

PREPARATION 126.—**Benzyl Alcohol** [*Phenyl-methanol*].

$$C_6H_5.CH_2OH. \qquad C_7H_8O. \qquad 108.$$

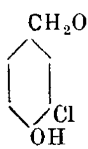
10 gms. (1 mol.) of benzyl chloride are refluxed with 10 gms. (excess) of potassium carbonate in 100 c.cs. of water until the smell of benzyl chloride disappears (about 6 hours). The liquid is extracted with ether, the extract dehydrated by standing 8 hours over anhydrous potassium carbonate, filtered into a small distilling flask, and the ether removed on a water bath. Distillation is continued with an air condenser over wire gauze, the fraction 200°—210° being collected separately.

$$2C_6H_5CH_2Cl + K_2CO_3 + H_2O = 2C_6H_5CH_2OH + 2KCl + CO_2.$$

*Yield.*—70% theoretical (7 gms.). Colourless liquid; aromatic odour; somewhat soluble in water; miscible in all proportions with alcohol and ether; B.P. 206·5°; D. $^{0}_{4}$ 1·0628; D. $^{15\cdot4}_{4}$ 1·05. (B., 25, 3290.)

The use of water in the hydroxylation of compounds containing a mobile halogen atom is illustrated in the following two preparations.

PREPARATION 127.—**3-Chloro-4-hydroxybenzyl Alcohol.**



$C_7H_7O_2Cl.$ 158·5.

10 gms. (1 mol.) of 3-chloro-4-hydroxybenzyl chloride are refluxed for 1 hour with 100 c.cs. of water. The cooled mixture is extracted with ether, the ether removed on a water bath and the oil which remains scratched with a glass rod until it crystallises. The crystals are pressed on a porous plate and recrystallised from benzene.

$$C_6H_3(CH_2Cl)(Cl)(OH)[1:3:4] + H_2O =$$
$$C_6H_3(CH_2OH)(Cl)(OH)[1:3:4] + HCl.$$

Colourless needles; insoluble in water, soluble in hot benzene and in ether; M.P. 123°. (B., 34, 2459.)

It will be observed that the nuclear halogen atom in the above compound is not replaced in the reaction.

PREPARATION 128.—**Glycollic Acid** [*Ethanol Acid*].

$$CH_2(OH)COOH. \qquad C_2H_4O_3. \qquad 76.$$

20 gms. (1 mol.) of potassium chloroacetate or potassium bromoacetate are dissolved in 80 c.cs. (excess) of water, and the solution *exactly* neutralised with sodium carbonate solution, and refluxed for 16 hours—porcelain chips being added to prevent bumping. It is cooled and concentrated to half its bulk under reduced pressure. The potassium halide which has separated is filtered off, and the filtrate evaporated to dryness under reduced pressure. The residue is extracted in a reflux apparatus with 50 c.cs. of boiling acetone and the extract evaporated to dryness on a bath kept at 65°.

$$CH_2Cl.COOK + H_2O = CH_2(OH)COOH + KCl.$$

*Yield.*—80% theoretical (13 gms.). Colourless deliquescent crystals; soluble in water and in acetone; M.P. 80°; K = 0·0152. The presence of the carboxyl group renders halogen atoms attached to the α-carbon labile and easily replaceable.

The above compound can also be prepared by boiling chloroacetic acid with an aqueous suspension of chalk (B., 16, 2954).

PREPARATION 129.—**Ethylene Glycol** [1 : 2-*Ethandiol*].

$$\begin{array}{l} CH_2OH \\ | \\ CH_2OH. \end{array} \qquad C_2H_6O_2. \qquad 62.$$

*By-product:* [1 : 2 : 2-*Tribromethan*].

$$\begin{array}{l} CH_2Br \\ | \\ CHBr_2. \end{array} \qquad C_2H_3Br_3. \qquad 267.$$

*Method I.*—9·4 gms. (1 mol.) of ethylene dibromide (see p. 339) are refluxed with 6·9 gms. (1 mol.) of pure potassium carbonate dissolved in 50 c.cs. of water. From the top of the reflux condenser a glass tube is led to a couple of wash bottles containing bromine. Some porcelain chips are added to the mixture to facilitate ebullition. When all the oily drops have disappeared (8—10 hours) the same quantities of ethylene dibromide and potassium carbonate are added to the solution, and the boiling continued as before. The operation is prolonged until 56·4 gms. of ethylene dibromide have been decomposed. After the third addition of ethylene dibromide, crystals of potassium bromide separate out on standing overnight. These, and those which separate out after each succeeding operation, are removed by filtration at the pump before the action is restarted. The crystals are then washed with absolute alcohol, the washings being subsequently used for the isolation of glycol (see p. 202). After decomposition of the ethylene dibromide is complete, the solution of glycol is heated on a water bath at 50° under reduced pressure in the apparatus shown on p. 28, so as to distil off the water slowly. When the distillation has

continued for some time, the liquid begins to bump violently, owing to the separation of the potassium bromide. The solution is cooled, the crystals of potassium bromide removed as before, and the distillation continued. When the solution becomes very viscid, and the temperature of the vapour passing over begins to rise, the distillation is stopped, and the residue is mixed with the alcohol used for washing the potassium bromide crystals, as explained above. After standing for some time, the crystals of potassium bromide which separate in quantity are removed by filtration at the pump, washed with absolute alcohol, and the combined alcoholic extracts concentrated by slow distillation as before from a flask fitted with a column. The residue is treated with absolute alcohol which precipitates more potassium bromide; this treatment is repeated, using a mixture of alcohol and ether, until all the potassium bromide has been removed. The solvent is removed by evaporation as above, and the residual glycol twice fractionated, at first under reduced pressure, and finally at the ordinary pressure.

$$\begin{array}{l} CH_2Br \\ | \\ CH_2Br \end{array} + K_2CO_3 + H_2O = \begin{array}{l} CH_2.OH \\ | \\ CH_2.OH \end{array} + 2KBr + CO_2.$$

*Yield.*—50% theoretical (10 gms.). Colourless viscid liquid; sweet taste; blue in thick layers in transmitted light; miscible with water in all proportions; D. $^{20}_{4}$ 1·134.

*Isolation of By-product.*—During the reaction, vinyl bromide ($CH_2:CHBr$) is formed. It volatilises and is absorbed by the bromine in the wash bottles. The product is washed with dilute caustic soda until excess bromine is removed; on fractionating, tribromoethane is obtained (B.P. 187°).

$$\begin{array}{l} CH_2Br \\ | \\ CH_2Br \end{array} \longrightarrow \begin{array}{l} CH_2 \\ \| \\ CHBr \end{array} + HBr.$$

$$\begin{array}{l} CH_2 \\ \| \\ CHBr \end{array} + Br_2 = \begin{array}{l} CH_2Br \\ | \\ CHBr_2. \end{array}$$

(J. C. S., 69, 176; J. pr., 11, 229; A., 192, 257; C., (1907), 1, 1314.)

The above method is necessary where a good yield of glycol is required. If yield is not a pressing consideration, the process may be shortened by refluxing all the materials together from the beginning, evaporating at 80° under reduced pressure until little more distils, extracting the residue twice with absolute alcohol, removing the alcohol under reduced pressure and fractionating the product.

Both these methods suffer from the difficulty of separating glycol from a large excess of water without loss. There is, however, a second method available for replacing halogen by hydroxyl. It consists in preparing an ester of the desired alcohol by heating the halide with certain salts—silver, potassium, or sodium acetate—and saponifying the ester so formed.

$$\begin{array}{l} CH_2Br \\ | \\ CH_2Br \end{array} + 2CH_3COOK = \begin{array}{l} CH_2.OOCCH_3 \\ | \\ CH_2.OOCCH_3, \end{array} + 2KBr.$$

For saponification, the ester is usually treated with hydrogen chloride dissolved in anhydrous methyl alcohol.

$$\begin{array}{l} CH_2.OOC.CH_3 \\ | \\ CH_2.OOC.CH_3 \end{array} + 2HCl = \begin{array}{l} CH_2OH \\ | \\ CH_2OH \end{array} + 2CH_3COCl.$$

The acetyl chloride reacts with the methyl alcohol forming methyl acetate and a fresh quantity of hydrochloric acid.

$$CH_3COCl + CH_3OH = CH_3COOCH_3 + HCl.$$

This method has a wide application, but it is especially useful for the preparation of glycol.

*Method II.*—200 gms. of pure potassium acetate are fused in a shallow dish, as described on p. 509, except that, unlike sodium acetate, the crystals contain no water of crystallisation, and only melt once. The solidified salt is finely powdered, and while still warm placed in a desiccator.

60 gms. (1 mol.) of ethylene dibromide (see p. 339), 20 gms. (excess) of glacial acetic acid, and 60 gms. (excess) of freshly fused, finely powdered potassium acetate are refluxed in a 500-c.c. flask for 2 hours, and the reaction product distilled, using a condenser. The distillate is again treated with 60 gms. (1 mol.) of ethylene dibromide, and 80 gms. (excess) of freshly fused, finely powdered potassium acetate, refluxed for 3 hours as before, and again distilled, using a good fractionating column (see p. 22), the fractions (1) 140°, (2) 140°—175°, (3) above 175°, being collected separately. The last two fractions are redistilled, the fraction 180°—190° being retained. The portion under 180° is again treated with 80 gms. of potassium acetate, refluxed and distilled as before. The total yield of glycol diacetate is about 90% theoretical (88 gms.). It boils at 180°.

40 gms. (excess) of pure anhydrous methyl alcohol (see p. 213) are cooled in water, and gaseous hydrogen chloride (see p. 506) led in until an increase in weight of 1 gm. has been obtained. Should a greater increase be found, the required $2\frac{1}{2}\%$ solution is obtained by adding the requisite quantity of pure anhydrous methyl alcohol. The 41 gms. of 2·5% alcoholic hydrogen chloride are refluxed with 50 gms. (1 mol.) of glycol diacetate on a water bath for 30 minutes, and the reaction mixture immediately distilled from the same bath. Methyl alcohol and methyl acetate are thus removed, the residue consisting of glycol and a small quantity of acetate, two substances the boiling points of which lie close together. They are separated by extraction with an equal volume of dry ether, glycol remaining undissolved. It is removed and fractionated, the temperature being slowly raised to 100°. The fraction 192°—198° is redistilled.

$$\begin{array}{l} CH_2Br \\ \dot{C}H_2Br \end{array} + 2CH_3COOK = \begin{array}{l} CH_2.O.COCH_3 \\ \dot{C}H_2.O.COCH_3 \end{array} + 2KBr.$$

$$\begin{array}{l} CH_2OCOCH_3 \\ | \\ CH_2OCOCH_3 \end{array} = 2HCl + 2CH_3OH = \begin{array}{l} CH_2OH \\ | \\ CH_2OH \end{array} + 2CH_3COOCH_3 + 2HCl.$$

*Yield.*—85% theoretical (18 gms.) on the glycol diacetate taken ; 75% theoretical on the ethylene dibromide originally taken (2·4 per 10 of ethylene dibromide). (*Cf.* yield by Method I. See p. 201.)

(See Gattermann, " Practical Methods of Organic Chemistry.")

The next preparation illustrates the activating effect of aromatic nitro groups on nuclear halogen atoms in the *o*- and *p*-positions.

PREPARATION 130.—**2 : 4-Dinitrophenol** (2 : 4-*Dinitro*-1-*hydroxybenzene*).

$$OH.C_6H_3(NO_2)_2[1:2:4]. \qquad C_6H_4O_5N_2. \qquad 184.$$

10 gms. (1 mol.) of chlorodinitrobenzene [1 : 2 : 4] are refluxed with 15 gms. (excess) of anhydrous sodium carbonate and 150 c.cs. of water until solution has occurred, cooled and acidified with dilute hydrochloric acid ; the precipitate is filtered, washed, and dried on a porous plate.

$$2Cl.C_6H_3(NO_2)_2[1:2:4] + Na_2CO_3 + H_2O = $$
$$2OH.C_6H_3(NO_2)_2[1:2:4] + 2NaCl + CO_2.$$

*Yield.*—90% theoretical (8 gms.). Colourless crystals ; insoluble in water ; M.P. 114°. (Z. Ch., (1870), 232.)

**Reaction LXXII. Replacement of the Diazonium Group by Hydroxyl.** (B., 22, 335 ; 23, 3705 ; 24, 1960 ; J. pr., 14, 451 ; A., 137, 39 ; D.R.P., 167211.)—This is a reaction of great importance in the aromatic series, both in the laboratory and on a manufacturing scale. When diazonium salts, especially the sulphate, are boiled with water or acids, nitrogen is evolved, and the phenol corresponding to the diazonium compound is formed. It is not necessary to isolate the diazonium salt ; the solution prepared in the usual way from the amine is boiled or slowly added to boiling dilute sulphuric acid, or an aqueous solution of sodium nitrite may be added to a boiling solution of the amine in dilute sulphuric acid. The use of the diazonium nitrate is to be avoided, as simultaneous nitration usually occurs. The reaction can be applied to substituted amines, amino-acids, amino-halogen compounds, etc., but the yields are often poor, especially with the amino-phenols ; they may be improved to some extent by the use of copper sulphate solution. Although the method is of practical importance only in the aromatic series, since aliphatic diazo-compounds are not found except at very low temperatures, yet aliphatic hydroxy compounds are readily obtained by the action of aqueous sodium nitrite solution on acid solutions of the primary amines. This reaction should be compared with the formation of ethers as by-products in the reduction of diazonium compounds with alcohol (Reaction, p. 376).

$$C_6H_5.N_2.SO_4H + H_2O = C_6H_5OH + N_2 + H_2SO_4.$$

PREPARATION 131.—**Phenol** (*Hydroxybenzene*).

$$C_6H_5.OH. \qquad C_6H_6O. \qquad 94.$$

20 gms. (1 mol.) of freshly distilled aniline are dissolved by gentle warming in 150 gms. of 30% sulphuric acid, and the cooled liquid treated with a 20% solution of sodium nitrite until a sample colours starch-iodide paper (see p. 504) ; some 16 gms. of $NaNO_2$ will be required. The whole

is kept at 50° for an hour, steam distilled until no more phenol distils (this is shown by a sample of the distillate giving no precipitate with bromine water), the distillate is saturated with salt, extracted several times with ether until nothing more is removed, and the extract dried for 24 hours over fused sodium sulphate. The ether is removed on a water bath and the residue distilled, the fraction 175°—185° being retained.

$$C_6H_5NH_2 \xrightarrow{H_2SO_4 + NaNO_2} C_6H_5.N_2.SO_4H \xrightarrow{H_2O} C_6H_5OH.$$

*Yield.*—35% theoretical (7 gms.). Colourless needles; characteristic odour; somewhat soluble in water; soluble in alcohol and ether; M.P. 40·8°; B.P. 182°. (B., 23, 3705; A., 137, 39; J. pr., 14, 451.)

If the residue in the flask after the steam distillation is filtered hot, and cooled, crystals of *p*-hydroxydiphenyl separate. It is formed by the coupling of a portion of the phenol first formed with undecomposed diazonium compound.

$$C_6H_5.N_2.SO_4H + H.C_6H_4OH = C_6H_5.C_6H_4OH + H_2SO_4 + N_2.$$

(*Cf.* p. 376.)

The yield is low owing to the heating with the mineral acid tending to cause resinification of the phenol. It has been suggested that heating with a weak acid, *e.g.*, boric acid, would prevent this, but no great improvement in the yield is obtained.

In an exactly similar manner from 20 gms. of *o*-, *m*- or *p*-toluidine, *o*-, *m*- or *p*-cresol respectively is prepared; for these it is better to use only 10% sulphuric acid, a quantity being taken equivalent to the 30% acid employed above. The yields are about 50% (12·5 gms.).

The melting and boiling points of the cresols are:

| | M.P. | B.P. |
|---|---|---|
| *o*-Cresol | 31° | 191° |
| *m*-Cresol | — | 202° |
| *p*-Cresol | 36° | 202° |

For the separation of *m*- and *p*-cresols, see C. r., 192, 1657.

The method is often important in the preparation of hydroxy derivatives of compounds the groups in which render them difficult to prepare by more direct means. *m*-Hydroxybenzoic acid is such a compound. It is obtained by nitration of benzoic acid followed by reduction to *m*-aminobenzoic acid and application of the present reaction (see below).

PREPARATION 132.—***m*-Hydroxybenzoic Acid** (*1-Hydroxy-3-carboxybenzene*).

$$C_6H_4(OH)(COOH)[1:3]. \qquad C_7H_6O_3. \qquad 138.$$

10 gms. (1 mol.) of *m*-aminobenzoic acid hydrochloride are dissolved in 100 c.cs. of water (or 8 gms. of the free acid are dissolved in 200 c.cs. of 2% hydrochloric acid) and a 30% aqueous solution of 5 gms. (excess) of sodium nitrite slowly added. The whole is warmed until nitrogen ceases to be evolved, filtered at the pump and evaporated until, on

cooling, crude *m*-hydroxybenzoic acid separates as a brown mass. It is purified by recrystallisation from water with addition of animal charcoal.

$$C_6H_4(NH_2)(COOH)[1:3] \xrightarrow{HNO_2} C_6H_4(OH)(COOH)[1:3].$$

*Yield.*—60% theoretical (7 gms.). Colourless crystals; soluble in hot water; M.P. 200°. (A., 91, 189.)

Certain di-amino compounds can also be made to yield di-hydroxy compounds in this way.

PREPARATION 133.—**4 : 4′-Dihydroxydiphenyl.**

$[4]OH.C_6H_4.C_6H_4.OH[4']$. $C_{12}H_{10}O_2$. 186.

50 gms. (1 mol.) of benzidine (see p. 160) are dissolved in 900 c.cs. (2 mols.) of 2% hydrochloric acid, and 5 litres (excess) of 5% sulphuric acid added. The mixture is diazotised, as described on p. 372, with 20% aqueous sodium nitrite. About 40 gms. of sodium nitrite will be required. Steam is passed into the solution for 30 minutes, and until a sample gives no precipitate with an alkaline solution of phenol. The diphenyl derivative is precipitated, filtered hot, and crystallised from boiling water, in which it is not very soluble.

$$[4]HN_2.C_6H_4.C_6H_4.NH_2[4'] \xrightarrow{HNO_2 + H_2SO_4} [4]OH.C_6H_4.C_6H_4OH[4'].$$

*Yield.*—55% theoretical (27 gms.). Colourless needles; M.P. 275°. (B., 22, 335.)

The next preparation illustrates the use of copper sulphate solution.

PREPARATION 134.—**Quinol** (1 : 4-*Dihydroxybenzene*).

$C_6H_4(OH)_2[1:4]$. $C_6H_6O_2$. 110.

30 gms. (1 mol.) of *p*-aminophenol are diazotised, as described on p. 372, and the diazonium solution slowly added to 400 gms. boiling 25% copper sulphate solution. When the evolution of nitrogen ceases the solution is cooled and extracted with ether until nothing further is removed. The ether is evaporated on a water bath, and the residue recrystallised from dilute sulphuric acid with the addition of a little animal charcoal.

$$C_6H_4(OH)(NH_2)[1:4] \xrightarrow{HNO_2} C_6H_4(OH)_2[1:4].$$

*Yield.*—30% theoretical (9 gms.). Colourless prisms; soluble in hot water, in ether, and in alcohol; M.P. 169°; sublimes at a moderate heat. (D.R.P., 167211.)

*o*-, *m*- and *p*-cresols (see p. 205) are obtained from the corresponding toluidines in an exactly similar way.

Catechol (*o*-dihydroxybenzene, M.P. 104°; B.P. 245°) is prepared in the same manner from *o*-aminophenol, a 10% solution of copper sulphate being employed. (See also O. S., III., 27.) Below is illustrated the effect of boiling a diazonium nitrate with water.

PREPARATION 135.—**3-Nitro-4-hydroxytoluene.**

$C_6H_3(CH_3)(OH)(NO_2)[1:4:3]$. $C_7H_7O_3N$. 153.

50 gms. (1 mol.) of finely powdered *p*-toluidine are dissolved in 500 gms. (excess) of warm 10% nitric acid (D = 1·06), and the solution diazotised at 0°, as described on p. 372, a 30% aqueous solution of 30 gms. of sodium nitrite being added until the solution colours starch-iodide paper; on no account must the temperature rise above 8°. After standing for 3 hours at 0°, 50 c.cs. of the solution are slowly heated in a litre round flask in an oil bath under a long reflux condenser until ebullition occurs and interaction commences. When the reaction is complete the remainder of the diazonium solution is *slowly* added, the boiling continued for 10 minutes, and the solution steam distilled until no further oil comes over. The solid nitro-cresol is filtered from the distillate, well washed with water, and purified by precipitation from an alkaline solution of its sodium salt, using dilute hydrochloric acid.

$$C_6H_4(CH_3)(NH_2)[1:4] \xrightarrow[HNO_3]{HNO_2} C_6H_3(CH_3)(OH)(NO_2)[1:4:3].$$

*Yield.*—60% theoretical (40 gms.). Yellowish crystals; insoluble in water; M.P. 36·5°. (B., 24, 1960.)

**Reaction LXXIII. Direct Replacement of the Aromatic Amino-group by Hydroxyl.** (B., 7, 77, 809; D.R.P., 109102.)—The simple primary amino-groups in the benzene series are not easily replaced directly by hydroxyl unless an activating group (*e.g.*, $NO_2$) be present in the *o*- or *p*-position. α-Naphthols, however, are readily obtained by heating α-naphthylamine derivatives with fairly concentrated acid under pressure.

$$C_{10}H_7NH_2 + H_2O = C_{10}H_7OH + NH_3.$$

(This reaction can be reversed, see p. 301.)

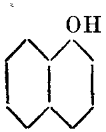
It can be accomplished more readily by heating with sodium bisulphite solution, an unstable naphthol-sulphite being an intermediate product. β-Compounds also react.

$$C_{10}N_7NH_2 + H_2SO_3 = C_{10}H_7O.SO_2H + NH_3.$$
$$C_{10}H_7O.SO_2H + H_2O = C_{10}H_7OH + H_2O + SO_2.$$

This reaction is of technical importance, being applied to the preparation of some hydroxy-sulphonic acids.

With *p*-nitroso-secondary and -tertiary bases the alkyl amino group can readily be replaced by boiling with dilute alkali. This method, too, is illustrated below.

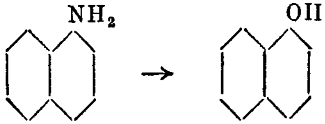
PREPARATION 136.—α-**Naphthol** (1-*Hydroxynaphthalene*).



$C_{10}H_8O$. 144.

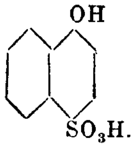
150 gms. (1 mol.) of α-naphthylamine (see p. 358) are heated, with 120 gms. (excess) of conc. sulphuric acid and 1 litre of water, to 200° for 8 hours at 14 atmospheres in an enamelled autoclave (see p. 45) fitted with a stirrer. On cooling, the autoclave is opened and α-naphthol filtered

off, washed, and recrystallised from water, or distilled preferably under reduced pressure.



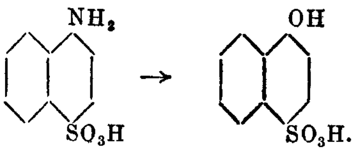
*Yield.*—95% theoretical (140 gms.). Colourless crystals; characteristic odour; sparingly soluble in water; M.P. 94°; B.P. 280°; is an important intermediate for dyestuffs. (D.R.P., 76545.)

PREPARATION 137.—**Nevile and Winther's Acid** (1-*Hydroxy*-4-*naphthalenesulphonic Acid*).



$C_{10}H_8O_4S$. 224.

100 gms. (1 mol.) of naphthionic acid (100%) (or the equivalent of sodium naphthionate), dissolved in 200 c.cs. of water, are refluxed for 24 hours with 600 gms. (excess) of sodium bisulphite solution (25% $SO_2$). 30% caustic soda solution is added until the solution is alkaline to phenolphthalein, and the whole boiled until no more ammonia is evolved. Hydrochloric acid is then added until the product is permanently acid. The Nevile and Winther's acid crystallises on cooling. It is separated from unchanged naphthionic acid by recrystallisation from warm water. It may be obtained as its sodium salt by neutralising the warm solution with caustic soda, and saturating with common salt.



*Yield.*—80% theoretical (80 gms.). Colourless crystals; soluble in hot water; decomposes on heating; important intermediate for azo dyestuffs. (B., 24, 3157; 27, 3458; A., 273, 102; D.R.P., 109102.)

PREPARATION 138.—*p*-**Nitrosophenol** (1-*Hydroxy*-4-*nitrosobenzene*).

$C_6H_4(OH)(NO)[1:4]$. $C_6H_5O_2N$. 123.

5 gms. (1 mol.) of *p*-nitrosodimethylaniline hydrochloride (see p. 285) are added gradually to 250 gms. (excess) of boiling $2\frac{1}{2}$% caustic soda solution in a flask fitted with a reflux condenser, the free base which separates as an oil being allowed each time to dissolve before the next addition. The boiling is continued after complete addition until the solution has become reddish-yellow. When cold, the liquid is acidified and extracted with ether, and the latter removed on a water bath. The residual nitrosophenol is redissolved in a little boiling water, and after filtration and

cooling it is again extracted with ether and recovered by evaporation of the ether.

$$NO.C_6H_4.N(CH_3)_2[1:4] + H_2O = NO.C_6H_4OH + NH(CH_3)_2.$$
$$NOC_6H_4OH \rightleftarrows HON:C_6H_4:O.$$

*Yield.*—90% theoretical (3·5 gms.). Colourless rhombic crystals; soluble in water, and in ether; M.P. 125°. (B., 7, 809.)

This reaction is frequently applied to the preparation of dialkylamines. The dimethylamine evolved in the above reaction may be absorbed by leading through hydrochloric acid; from the latter solution the hydrochloride is obtained by evaporation. *p*-Nitrosophenol, it is to be noted, is tautomeric, in some reactions behaving as quinone monoxime.

**Reaction LXXIV.** (*a*) **Action of Mineral Acids on Phenylhydroxylamine.** (B., 26, 1844, 2810; 27, 1927; 20, 3040.)—In the presence of mineral acids phenylhydroxylamine undergoes rearrangement to form *p*-aminophenol.

$$C_6H_5NH.OH \rightarrow OH.C_6H_4NH_2.$$

This isomerisation explains the course of the electrolytic reduction of aromatic nitro compounds (see p. 399), also the oxidation of aniline to quinone (see p. 235).

PREPARATION 139.—***p*-Aminophenol** (1-*Hydroxy*-4-*aminobenzene*)

$$C_6H_4(OH)(NH_2)[1:4] \quad C_6H_7ON. \qquad 109.$$

5 gms. of phenylhydroxylamine (see p. 369) are slowly added to 100 c.cs. of 50% sulphuric acid, cooled in a freezing mixture, 500 c.cs. of water poured in, and the whole boiled until a sample, tested with chromic acid solution, gives a smell of quinone and no smell of nitrobenzene. The liquid is neutralised with sodium bicarbonate, saturated with common salt, and extracted with ether. The ether is removed by evaporation, and the residue washed with cold water and dissolved in hot water. The solution is filtered hot, and cooled, and the *p*-aminophenol again extracted with ether.

$$C_6H_5NHOH \rightarrow OH.C_6H_4.NH_2.$$

*Yield.*—Almost theoretical (5 gms.). Colourless crystals; somewhat soluble in water; M.P. 185°. (B., 26, 1844, 2810; 27, 1927; 29, 3040.)

**Reaction LXXIV.** (*b*) **Transformation of Azoxy Compounds to Azophenols.** Azoxy compounds (see Reaction CLXX.) are converted by conc. sulphuric acid into *p*-hydroxyazo compounds (B., 13, 525).

$$\underset{\diagdown_{O}\diagup}{C_6H_5N\text{——}NC_6H_5} \rightarrow HOC_6H_4N = NC_6H_5.$$

Most azoxy compounds under the influence of ultra-violet light are converted into *o*-hydroxyazo compounds. (J. C. S., 127, 2374.)

The transformation takes place as follows:

$$C_6H_5N\underset{\diagdown O \diagup}{——}NC_6H_5 \rightarrow C_6H_5\underset{\underset{O}{\downarrow}}{N} = NC_6H_5 \rightarrow HOC_6H_4N = NC_6H_5.$$

The *unsym.* azoxy compound has been isolated by the action of light on $\alpha\alpha'$-azoxynaphthalene (J. C. S., 123, 2466). When the latter is heated with benzaldehyde the *unsym.* azoxy compound is also formed, whilst if a base such as quinoline is present, the further transformation to the *o*-hydroxyazo compound takes place.

**Reaction LXXV. Fusion of Aromatic Sulphonic Acids with Caustic Alkalis.** (Z. Ch., (1876), 3, 299; J. pr., [2], 17, 394; 20, 300.)—This method is of technical importance as it is employed to prepare phenols and naphthols from the parent hydrocarbons. These phenols and naphthols are much used as intermediates in the dye industry. The method cannot easily be applied to determine structure, owing to rearrangement liable to occur at the elevated temperatures. Caustic potash is more convenient than soda, since it generally yields a more easily fusible mixture.

PREPARATION 140.—**Phenol** (*Hydroxybenzene*).

$$C_6H_5OH. \qquad C_6H_6O. \qquad 94.$$

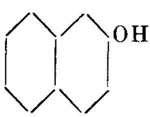
100 gms. of caustic soda and 10 c.cs. of water are heated in an iron or nickel basin (or in a glue-pot, Fig. 53) to 290°. 130 gms. of sodium benzene sulphonate are gradually added, care being taken that the temperature is maintained between 290° and 300°, the mass being stirred with a thermometer pocket (see below). After the addition, the temperature is raised to 330° (but not beyond 340°) and maintained for 15 minutes. The melt is cooled, then dissolved in the minimum of water and transferred to a beaker, where it is carefully acidified under good cooling with conc. hydrochloric acid. After three extractions with ether the combined extracts are dried with anhydrous sodium sulphate for 24 hours. The ether is then distilled off and the residue fractionated at 175°—185°.

$$C_6H_5SO_3K \rightarrow C_6H_5OK \rightarrow C_6H_5OH.$$

*Yield.*—70% theoretical (6·5 gms.). Colourless needles; characteristic odour; somewhat soluble in water; soluble in alcohol and ether; M.P. 40·8°; B.P. 182°. (Z. Ch., (1867), 3, 299; J. pr., 20, 300; Abs. B., 1935, 91.) See U.S.P., 1789071.

For dealkylation of cresols to phenol under pressure, see E.P., 427145.

PREPARATION 141.—**$\beta$-Naphthol** (2-*Hydroxynaphthalene*).



$$C_{10}H_8O. \qquad 144.$$

200 gms. (excess) of solid caustic soda free from chloride, and 60 c.cs. water are placed in a fusion-pot (Fig. 53), which consists of a glue-pot, the outer pot containing the Pb-Sn eutectic mixture (p. 39). The thermometer is placed inside the iron tube containing a little mercury at the bottom, and this tube is used as stirrer. The pot is heated

until the temperature is 270°. 300 gms. of dry powdered sodium $\beta$-naphthalene sulphonate are then gradually added, the temperature being allowed to rise to 290° when half of the salt has been added, to 300° when three-quarters has been added, and to 305° when all has been added, and finally to 318°—but no higher—for 15 minutes. The melt, after cooling somewhat, is poured into 2 litres of water with continual stirring (*caution!*). The solution is acidified with 50% sulphuric acid, and boiled to expel sulphur dioxide, an indicator being used to show final acidity in the solution. The $\beta$-naphthol is then filtered off, washed with water and dried. It may be recrystallised from hot water.

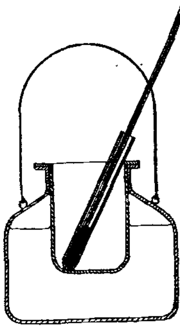


FIG. 53.

$$C_{10}H_7SO_3Na \rightarrow C_{10}H_7ONa \rightarrow C_{10}H_7OH.$$

*Yield.*—70% theoretical (130 gms.). Colourless crystals with characteristic odour; M.P. 122°; B.P. 286°. Important intermediate for dyestuffs.

$\alpha$-Naphthol (M.P. 94°; B.P. 280°) is prepared from sodium $\alpha$-naphthalene-sulphonate in an exactly similar manner. For the preparation of alizarin by the application of the same reaction, see p. 391.

**Reaction LXXVI. Addition of Hydroxyl to Ethylenic Bonds.** (B., 21, 919; A., 268, 27.)—When compounds containing ethylenic linkages are treated with mild oxidising agents, *e.g.*, bromine and caustic potash, dilute nitric acid and especially very dilute (2%) potassium permanganate solution, addition of hydroxyl at the double bond to form a 1 : 2-dihydroxy compound occurs.

$$R_1CH : CHR_2 \xrightarrow{O_2 + H_2O} R_1CHOHCHOHR_2.$$

If stronger oxidising agents are employed the carbon chain can be broken at that point.

$$R_1CHOHCHOHR_2 \xrightarrow{O_2} R_1COOH + R_2COOH.$$

This reaction is used to determine the presence and position of double bonds in organic compounds; it has been much applied to the elucidation of the structure of members of the terpene series.

Ethylene is catalytically hydrated to ethyl alcohol by steam at 100°—300°, the catalysts being salts of phosphoric acid. (E.P., 423877.)

PREPARATION 142.—**Phenyldihydroxypropionic Acid** [3-*Phenyl*-2 : 3-*propandiol Acid*].

$$C_6H_5.CHOH.CHOH.COOH. \qquad C_9H_{10}O_4. \qquad 182.$$

20 gms. (1 mol.) of cinnamic acid (see p. 113) are dissolved in 3 litres of 5% aqueous caustic soda and 2 litres (excess) of 2% aqueous potassium permanganate solution are added with good cooling and mechanical

stirring. The temperature must be kept at $-5°$ throughout. The liquid is filtered, nearly neutralised with 20% hydrochloric acid, and concentrated until the dissolved salts begin to separate. Neutralisation is then completed with conc. hydrochloric acid, and the product repeatedly extracted with large quantities of ether until nothing further is removed.

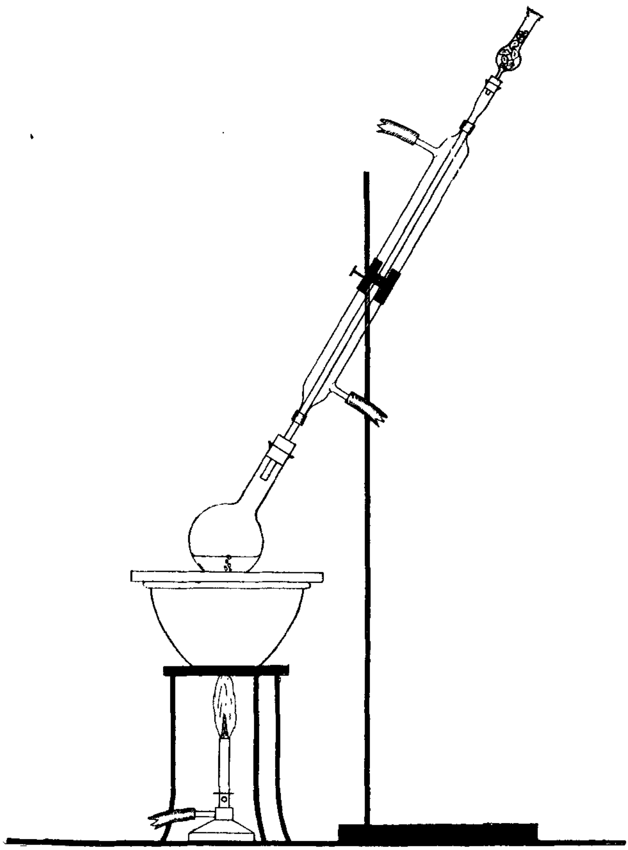


FIG. 54.

Owing to the solubility of phenyldihydroxypropionic acid in water this will necessitate at least ten extractions. The ethereal solution is evaporated, and the residue redissolved in ether, the solution filtered, and evaporated to low bulk. The pure acid separates on cooling.

$$C_6H_5CH : CHCOOH \xrightarrow{O_2} C_6H_5CH(OH)CH(OH)COOH.$$

*Yield.*—70% theoretical (17 gms.). Colourless needles; soluble in water; somewhat soluble in ether; M.P. 141°. (B., 21, 919; A., 268, 27.)

As this section contains the most important methods of preparing alcohols, processes for the purification of commercial methyl and ethyl alcohols are given here.

### Purification of Methyl Alcohol. [*Methanol*]

$CH_3OH$. $CH_4O$. 32.

Methyl alcohol, manufactured by the dry distillation of wood, is usually contaminated with acetone, its homologues and condensation products, and also with acetaldehyde, methyl acetate, dimethyl acetal, etc. It is purified by refluxing with 5% of solid caustic potash on a water bath and distilling. It is then allowed to stand for 24 hours over 40% freshly burnt quicklime, and redistilled from a water bath, the distillate being collected at 66°—67°. This removes all but the very last traces of water. If anhydrous methyl alcohol is required the product obtained above is boiled with about 1% of freshly prepared calcium turnings on a water bath, under a reflux condenser (see Fig. 54) fitted with a calcium chloride tube until the solid deposit, at first black, becomes almost white. It is then distilled into a receiver fitted with a calcium chloride tube, and the portion passing over at a constant temperature twice redistilled over 5% of calcium turnings, using a column. The solid formed should be white, and the alcohol all distil at a constant temperature. As the anhydrous alcohol is very hygroscopic it must not be exposed to air.

Colourless liquid; spirituous odour; miscible in all proportions with water; B.P. 66·5°; D. $^{20}_{4}$ 0·79133. (B., 41, 4322.)

Methyl alcohol of very high purity can be obtained by fractional distillation using a column of 1·3 metres effective length and then refluxing with aluminium amalgam. It is then refluxed under a column packed with dehydrated copper sulphate, to remove ammonia. A sensitive test for acetone and formaldehyde is the addition of conc. mercuric cyanide solution, in 6N-sodium hydroxide. A white precipitate indicates ketone; if it darkens on standing aldehyde is also present. (J. C. S., 127, 2552.)

### Purification of Ethyl Alcohol. [*Ethanol*]

$C_2H_5OH$. $C_2H_6O$. 46.

To prepare absolute alcohol, 100 gms. of freshly burnt quicklime in the form of small lumps are placed in a 500-c.c. distilling flask, and 300 gms. of rectified spirits added. After 8 hours the alcohol is distilled off on a water bath until a thermometer in the neck of the flask indicates 80°. The alcohol so obtained still contains about 3% of water.

To further purify the alcohol the above product is shaken with finely divided silver oxide. This oxidises any aldehyde present to acetic acid. Caustic soda is added to bind the acid, and the alcohol distilled, using a good column (see p. 22). The portion passing over at constant temperature is then treated with calcium turnings in the same way as methyl alcohol (see above). The anhydrous alcohol is very hygroscopic, and must not be exposed to air.

For the removal of the last traces of water the alcohol may be refluxed several hours with small quantities of sodium and ethyl succinate or phthalate. (J. C. S., 1927, 1288; Am. Soc., 1931, 1106.)

If the presence of methyl alcohol is permissible an effective method of drying consists in refluxing for several hours with magnesium methylate. (O. S., VII., 37.)

Colourless liquid; spirituous odour; miscible with water in all proportions; binary mixture with water contains 75·57% alcohol, and boils at 78·1° at 760 mms.; B.P. $^{760}$ pure alcohol, 78·3°; B.P. $^{21}$ 13°; D. $^{15}_{4}$ 0·790. It forms a ternary mixture with benzene and water, and this property is utilised in the manufacture of industrial absolute alcohol. (J. C. S., 81, 707; see Preparation 198; B., 38, 3612.)

# CHAPTER XIV

## OXYGEN TO CARBON

## Oxide Compounds

### Ethers

**Reaction LXXVII. Action of Sulphuric Acid on an Alcohol or a Mixture of Alcohols.** (J. Pharm., 1, 97; Phil. Mag., [3], 37, 350.)—This is the commercial method of obtaining diethyl ether from ethyl alcohol. The reaction occurs in two stages; an alkyl hydrogen sulphate is first formed and this yields ether on interaction with more alcohol.

$$C_2H_5OH + H_2SO_4 = C_2H_5.SO_4H + H_2O.$$
$$C_2H_5.SO_4H + C_2H_5OH = C_2H_5.O.C_2H_5. + H_2SO_4.$$

Thus, in theory, a limited quantity of sulphuric acid can convert an unlimited quantity of alcohol to ether, but in practice, owing to side reactions, this does not hold. Sulphuric acid may be replaced by phosphoric, arsenic, or benzene-sulphonic acid. By using a mixture of alcohols "mixed ethers" may be obtained. Simple ethers are formed simultaneously, however. For mixed ethers it is better to use the methods given on pp. 216, 217. As a catalyst in the above reaction, sand or aluminium sulphate may be employed. The method is applicable to naphthols, but not to phenols.

Preparation 143.—**Diethyl Ether.**

$$(C_2H_5)_2O. \qquad C_4H_{10}O. \qquad 74.$$

100 gms. of 90% alcohol are placed in a $\frac{1}{2}$-litre distilling flask, and under good cooling 180 gms. of conc. sulphuric acid are slowly added. The flask is fitted with a thermometer dipping into the liquid and an arrangement for admitting alcohol below the surface of the acid. The best arrangement consists of a separating funnel attached through a cork to a thistle funnel which forms part of the special apparatus (Fig. 8) and which is drawn out to a capillary and upturned. The flask is maintained at 140°—145° on a sand bath. Alcohol is run in from the tap funnel at the same rate as the liquid distils (two drops a second), until when about 150 gms. of alcohol have been added, heating is discontinued. The distillate is freed from sulphurous acid by shaking twice with 50 c.cs. of 10% caustic soda solution and from alcohol by shaking twice with the same quantity of saturated sodium chloride solution. The ether is dried for 24 hours over anhydrous calcium chloride, distilled on a water bath, and collected at 35°.

The yield is improved by adding 10% of its weight of anhydrous ferric chloride, aluminium sulphate, stannous sulphate or sand, to the mixture of sulphuric acid and alcohol. The ether obtained as above is pure enough for ordinary purposes; but, when pure, anhydrous ether is required, the last traces of alcohol and water are removed by allowing the ether to stand in a flask over metallic sodium in the form of thin slices or wire. The flask is fitted with a calcium chloride tube to allow hydrogen to escape and prevent the ingress of moisture. After 24 hours the ether is distilled over fresh metallic sodium. Owing to its volatility and inflammability ether should always be distilled from a water bath in the apparatus (p. 20) for the distillation of volatile liquids (see below).

*Yield.*—80% theoretical (100 gms.). Colourless liquid; characteristic odour; miscible with alcohol in all proportions; slightly soluble in water (1 in 10); B.P. $^{760}$ 34·49°; D. $^{15}_{4}$ 0·720. (J. Pharm., 1, 97; Phil. Mag., [3], 37, 350.)

### Purification of Commercial Ether

The chief impurities in commercial ether are alcohol and water, with traces of aldehyde, methyl alcohol, acetone, due to it being made from methylated spirit. It may be purified as above. The presence of alcohol may be proved by shaking with a spirit soluble dye, *e.g.*, aniline violet. If alcohol is present a blue solution is obtained. Water is detected by the cloudiness formed on mixing with carbon disulphide.

*N.B.*—Ether, which is kept in air and light, develops peroxides which are explosive and remain in the residue after distillation. These can usually be removed by shaking with permanganate solution or with silver nitrate and caustic potash solutions. Ether, therefore, should always be distilled from a water bath to avoid heating the residue to a high temperature.

**Reaction LXXVIII. Action of Alkyl Halides on Alkali Alcoholates or Phenates.** (P. R. S., 7, 135; J. C. S., 2, 198; A., 78, 226; 152, 164; B., 12, 116.)—This method is of importance as indicating the structure of ethers. It is applicable both in the aromatic and aliphatic series; and can be used to obtain the ethers corresponding to the hypothetical di- and tri-hydric-alcohols, in which more than one hydroxyl group is attached to one carbon.

$$CH_2Cl_2 + 2C_2H_5ONa = CH_2(OC_2H_5)_2 + 2NaCl.$$

PREPARATION 144.—**Phenetole** (*Ethoxybenzene*).

$$C_6H_5.O.C_2H_5. \qquad C_8H_{10}O. \qquad 122.$$

A 500-c.c. round flask containing 200 c.cs. (excess) of absolute ethyl alcohol is attached to a reflux condenser, and 8 gms. (1 mol.) of sodium in thin slices or in small pieces of wire are added. When it has completely dissolved 31 gms. (1 mol.) of phenol and 75 gms. (excess) of dry ethyl iodide are added, and the whole refluxed on a water bath until the solution

is no longer alkaline (4 hours). The alcohol and excess of ethyl iodide are distilled off on a water bath, the residue treated with water to dissolve sodium iodide, and extracted with ether. After drying over calcium chloride ether is removed on a water bath and the phenetole distilled over the naked flame, the distillate being collected between 168°—173°.

$$C_6H_5OH + C_2H_5ONa = C_6H_5ONa + C_2H_5OH.$$
$$C_6H_5ONa + C_2H_5I = C_6H_5.O.C_2H_5 + NaI.$$

*Yield.*—Almost theoretical (40 gms.). Colourless liquid; pungent smell; insoluble in water; B.P. 172°; D. $^{15}_{4}$ 0·973. (A., 78, 226.)

It should be noted that owing to the great affinity of the phenol for sodium, no sodium alcoholate remains to react with the ethyl iodide. Diethyl ether, however, may be prepared in a similar manner, using the same quantities of sodium, alcohol and ethyl iodide as above. The ether and excess of alcohol are distilled off and the ether separated from the alcohol by the addition of salt solution. Anisole (phenylmethyl ether, B.P. 154°, see p. 218) can also be prepared in a similar way, using corresponding quantities of methyl alcohol and methyl iodide. The alkyl iodides give the best yields, but alkyl chlorides can also be employed.

PREPARATION 145.—**Ethyl Orthoformate** (*Triethoxymethane*).

$$CH(OC_2H_5)_3. \qquad C_7H_{16}O_3. \qquad 148.$$

58·5 gms. (3 mols.) of metallic sodium, well pressed between filter paper, and cut into thin slices or pressed into wire (see p. 508), are placed in a dry flask of about 1½ litres capacity, and covered with a layer of anhydrous ether (see p. 216). The flask is connected to a condenser. A mixture of 117 gms. (3 mols.) of absolute alcohol and 100 gms. (1 mol.) of anhydrous chloroform is added drop by drop from a tap funnel. At the beginning the reaction is violent, and the flask must be well cooled with ice; sodium chloride separates and the liquid gradually changes to a brown colour. To complete the reaction the mass is warmed on a water bath until all the sodium present is converted into sodium chloride. The contents of the flask are poured into water, the ethereal solution of ethyl orthoformate which separates is removed, washed three times with water, dehydrated over calcium chloride, the ether removed on a water bath, and the residue distilled over a bare flame. That portion of the distillate which passes over above 100° is collected separately and redistilled, the fraction 143°—150° being retained.

$$CHCl_3 + 3C_2H_5ONa = CH(OC_2H_5)_3 + 3NaCl.$$

*Yield.*—70% theoretical (85 gms.). Colourless liquid; insoluble in water; soluble in ether; B.P. 145°—147°; D. $^{4}_{0}$ 0·8964. (P. R. S., 7, 135; J. C. S., 2, 198; A., 152, 164; B., 12, 116; O. S., V., 55.)

**Reaction LXXIX. Action of Dimethyl Sulphate on Hydroxy Compounds.** (A., 327, 114.)—Dimethyl sulphate is a valuable methylating agent, and can be used in all cases in place of methyl iodide. It reacts with greater readiness and gives better yields. The substance to be treated is dissolved

or suspended in cold conc. caustic potash solution and a slight excess of dimethyl sulphate added. Great care must be taken in working with dimethyl sulphate, as it is excessively poisonous (see p. 68).

$$RONa + (CH_3)_2SO_4 = ROCH_3 + NaCH_3SO_4.$$

This reagent has proved especially important in the study of the constitution of the sugars, and of cellulose. A series of methyl-celluloses has been obtained, and by the study of their hydrolysis, or decomposition in a vacuum, some light has been thrown on the structure of the cellulose molecule. (J. S. C. I., 41, 362 R.) In the laboratory dimethyl sulphate is much employed in the methylation of phenols and naphthols. Diethyl sulphate is not so suitable for such alkylations as its lower homologue.

PREPARATION 146.—**Anisole** (*Phenyl methyl ether*).

$$C_6H_5.O.CH_3. \qquad C_7H_8O. \qquad 108.$$

**Caution !**—*Dimethyl sulphate is very poisonous and this preparation must be carried out in a good fume cupboard.* (See p. 261.)

30 gms. (1 mol.) of phenol dissolved in 160 gms. (excess) of 10% aqueous caustic soda solution in a $\frac{1}{2}$-litre round-bottomed flask are *carefully* treated with 50 c.cs. of commercial dimethyl sulphate, and the whole continually shaken. The flask is closed by a cork through which passes a thermometer and a glass tube, bent in a spiral to prevent liquid spurting. The beginning of the reaction is shown by the separation of an upper layer of oil, and by the evolution of heat. The temperature must be kept between 40°—50°. When no more heat is evolved, excess of dimethyl sulphate is destroyed by boiling under a reflux condenser with frequent shaking. The liquid is cooled and caustic soda added until an alkaline reaction is obtained; the whole is extracted with ether and the extract dried by shaking with anhydrous potassium carbonate and filtered. The ether is removed on a water bath and the residue distilled, the fraction 150°—156° being retained.

$$C_6H_5OH + NaOH = C_6H_5ONa + H_2O.$$
$$C_6H_5ONa + (CH_3)_2SO_4 = C_6H_5.O.CH_3 + Na.CH_3.SO_4.$$
$$(CH_3)_2SO_4 + 2NaOH = 2CH_3OH + Na_2SO_4.$$

*Yield.*—90% theoretical (32 gms.). Colourless oil; pleasant odour; insoluble in water; soluble in ether; B.P. 154°; D. $^{15}_{4}$ 0·991. (A., 41, 71; 48, 65; 78, 226; 327, 114; O. S., IX., 12.)

Other methyl ethers may be prepared in a similar manner; *e.g.*, $\beta$-naphthyl methyl ether (M.P. 71°) is formed in good yield from $\beta$-naphthol.

The next preparation illustrates the preparation of the ethers of the polyhydric phenols.

PREPARATION 147.—**Pyrogalloltrimethyl Ether** (1 : 2 : 3-*Trimethoxybenzene*).

$$C_6H_3(OCH_3)_3[1:2:3]. \qquad C_9H_{12}O_3. \qquad 168.$$

**Caution !**—*Dimethyl sulphate is very poisonous. (See note to previous preparation.)*

20 gms. (1 mol.) of pyrogallol are dissolved in 30 gms. (excess) of 35% aqueous caustic soda in a 1-litre round-bottomed flask closed with a cork, through which pass a thermometer and an open tube bent in a spiral to prevent spurting. 50 c.cs. (excess) of commercial dimethyl sulphate are gradually added with continuous shaking, the cork being momentarily removed. The temperature is not allowed to rise above 45°. When heat is no longer evolved, the mixture is boiled under a reflux condenser, cooled, made alkaline with caustic soda if necessary, the dark-coloured precipitate filtered at the pump, and well washed with water. It is dissolved in ether, filtered, the ether removed on a water bath, and the residue recrystallised from dilute alcohol.

$$C_6H_3(ONa)_3[1:2:3] \xrightarrow{(CH_3)_2SO_4} C_6H_3(OCH_3)_3[1:2:3].$$

*Yield.*—70% theoretical (19 gms.). Colourless crystals; insoluble in water; soluble in alcohol and ether; M.P. 47°; B.P. 235°. (B., 21, 607, 2020, R., 126.)

PREPARATION 148.—β-**Naphthylmethyl Ether** (2-*Methoxynaphthalene*).

$OCH_3$. $C_{11}H_{10}O$. 158

(*See cautions to previous two preparations.*)

10 gms. (1 mol.) of β-naphthol are dissolved in 40 gms. (excess) of 10% caustic soda solution, and the cooled liquid mixed with 8 c.cs. of commercial dimethyl sulphate, as described in the two previous preparations. Gentle warming may be needed to start the reaction. The required ether separates as a solid which is filtered off after boiling and making alkaline if necessary, as before. The precipitate is washed with water and recrystallised from alcohol.

$$C_{10}H_7OH[2] \xrightarrow[NaOH]{(CH_3)_2SO_4} C_{10}H_7.OCH_3[2].$$

*Yield.*—Almost theoretical (11 gms.). Lustrous plates; insoluble in water; soluble in ether and in hot alcohol; M.P. 71°. (B., 26, 2706.)

The following preparations show the way in which cellulose, $[C_6H_7O_2(OH)_3]$, can be methylated to give compounds having the empirical composition:

$$[C_6H_7O_2(OH)_2(OCH_3)]_n,\ [C_6H_7O_2(OH)(OCH_3)_2]_n \text{ and } [C_6H_7O_2(OCH_3)_3]_n.$$

These compounds are known respectively as monomethyl cellulose, dimethyl cellulose, and trimethyl cellulose. It has not yet been proved, however, that they are definite chemical substances.

PREPARATION 149.—**The Methyl-celluloses.**—(i.) *Mono***methylcellulose.**

$(C_6H_7O_2(OH)_2(OCH_3))_n$. $(C_7H_{12}O_5)_n$. $176_n$.

50 gms. (1 mol.) of well-picked sliver cotton are shaken in a 2-litre flask closed as described in Preparation 147, with 180 c.cs. (excess) of

23% caustic soda; after standing for 1 hour the cotton is "pounded" in a glass mortar. It is returned to the flask, and 110 c.cs. (excess) of dimethyl sulphate gradually added (*caution!* see p. 68), the flask being shaken for $\frac{1}{2}$ hour between each addition. When no further evolution of heat occurs, the flask is filled with water and the contents poured through a 100-mesh copper gauze. The methyl cotton is well washed with water and dried in an air oven.

$$[C_6H_7O_2(OH)_3]_n \rightarrow [C_6H_7O_2(OH)_2(OCH_3)]_n$$

*Yield.*—Almost theoretical (53 gms.). The methyl cotton is best characterised by its methoxyl content (see p. 487), which should be close to 17·65% $OCH_3$.

(ii.) ***Di*methylcellulose.**

$$[C_6H_7O_2(OH)(OCH_3)_2]_n. \qquad (C_8H_{14}O_5)_n. \qquad 190_n.$$

50 gms. (1 mol.) of monomethyl cellulose, prepared as above, are treated as before with 175 c.cs. (excess) of 20% caustic soda solution and 120 c.cs. of dimethyl sulphate added. The subsequent operations are as above. The dried product contains about 28% $OCH_3$. 50 gms. of this latter product are treated with 400 gms. of water, and 100 c.cs. of 75% caustic soda solution added slowly and with shaking. 100 c.cs. of dimethyl sulphate are added under cooling. The subsequent operations are as in (i.)

$$(C_6H_7O_2(OH)_2(OCH_3))_n \text{——} [C_6H_7O_2(OH)(OCH_3)_2]_n.$$

*Yield.*—90% theoretical (48 gms.).

The product should contain close to 32·63% $OCH_3$.

(iii.) ***Tri*methylcellulose.**

$$[C_6H_7O_2(OCH_3)_3]_n. \qquad (C_9H_{16}O_5)_n. \qquad 204_n.$$

50 gms. (1 mol.) of dimethyl cellulose are treated with 100 gms. of water, and 140 c.cs. of 75% aqueous caustic soda solution slowly poured in, with good shaking and cooling. 120 c.cs. of dimethyl sulphate are added, and the whole allowed to stand overnight and filtered. 100 c.cs. of 75% aqueous caustic soda are poured in, and 120 c.cs. more of dimethyl sulphate added, as before. The subsequent operations are as in (ii.).

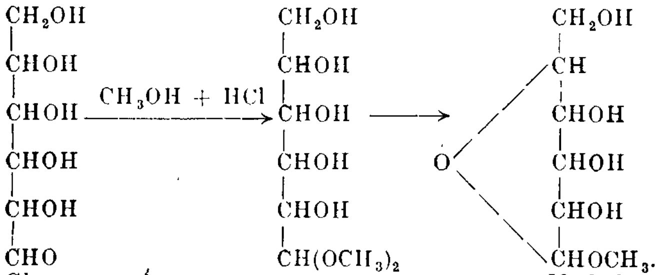
$$[C_6H_7O_2(OH)(OCH_3)_2]_n \text{——} [C_6H_7O_2(OCH_3)_3]_n.$$

*Yield.*—80% theoretical (45 gms.). The product contains about 42·5% methoxyl; the theoretical percentage for a trimethyl cellulose is 45·6%, but it is impossible to methylate cellulose completely. It will be noted how the strength of the caustic soda used varies with the percentage of methoxyl required in the product. (J. C. S., 103, 1735.)

By repetitions of the above procedures, methoxyl contents of 20·4% in (i.), 39·5% in (ii.), and 44·6% in (iii.) have been obtained. (J. C. S., 119, 77.)

**Reaction LXXX. Action of very Dilute Methyl Alcoholic Hydrogen Chloride on the Sugars.** (B., 28, 1151.)—When the hexoses are heated for a long time at 100° with very dilute methyl alcoholic hydrogen chloride, methyl glucosides are produced. This synthesis is important, as it

indicates methods for the synthesis of the higher sugars which are themselves of the glucoside type.



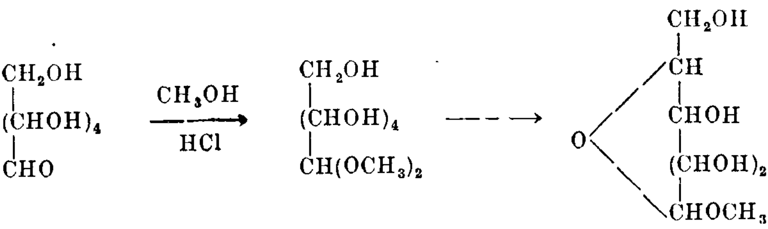
Glucose. Methyl-glucoside.

Each sugar can yield two glucosides ($\alpha$ and $\beta$), since the carbon to which the methoxyl group becomes attached is in that way rendered asymmetric. It is assumed that each sugar first forms a dimethyl-acetal, which loses alcohol to yield the glucoside. In the following preparation it is the $\alpha$-glucose which preponderates in the product.

PREPARATION 150.—$\alpha$-**Methyl-*d*-glucoside** [1-*Methoxy-pentol-hexan*].

$C_6H_{11}O_5.OCH_3$. $C_7H_{14}O_6$. 194.

10 gms. of methyl alcohol, dehydrated and purified as described on p. 213, are treated with dry gaseous hydrogen chloride until a little over 0·25 gm. has been absorbed, the flask being cooled in ice to prevent loss by evaporation. The liquid is then diluted with pure anhydrous methyl alcohol, so that it is exactly a 0·25% solution of hydrogen chloride in the alcohol. 25 gms. (1 mol.) of finely powdered anhydrous grape-sugar are then added to 100 gms. (excess) of the diluted solution, and the liquid refluxed for 1 hour until the sugar has all dissolved. The liquid now contains an intermediate product, possibly glucose-dimethyl-acetal; further heating in a sealed tube (see p. 41) at 100° for 60 hours transforms it to the glucoside. The sealed tube used should be a wide one and should be placed in a water bath, which is boiled behind a screen. The tube is then opened (see p. 44), the solution evaporated to about one-third of its volume, and placed in a freezing mixture. After standing a time, or sooner if "inoculated" with a small crystal, the $\alpha$-methyl-glucoside separates; it is filtered off after 12 hours. By prolonged heating of the mother-liquor to 100° with fresh 0·25% methyl-alcoholic hydrogen chloride a further yield of glucoside may be prepared. The whole product is recrystallised from ethyl alcohol.



*Yield.*—40% theoretical (10 gms.). Colourless needles; soluble in hot alcohol; M.P. 105°; $[\alpha]_D + 157{\cdot}6°$. (B., 28, 1151; 34, 2899; J. C. S., 1929, 300.)

**Reaction LXXXI. Action of Hydrogen Chloride on a Mixture of an Aldehyde and an Alcohol.** (B., 30, 3053; 31, 545.)—The reaction is of the same type as the preceding. Under the influence of condensing agents, calcium chloride, hydrogen chloride, etc., aldehydes combine with alcohols to yield the ethers of the hypothetical dihydroxy compounds from which the aldehydes are derived. Ketones form these compounds only with difficulty.

$$RCHO + 2R_1CH_2OH \rightarrow RCH(OCH_2R_1)_2 + H_2O.$$

PREPARATION 151.—**Diethylacetal** (1 : 1-*Diethoxyethane*).

$$CH_3CH(OC_2H_5)_2. \qquad C_6H_{14}O_2. \qquad 118.$$

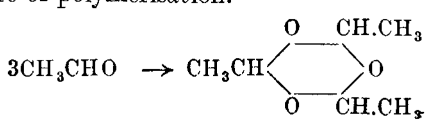
15 gms. of anhydrous calcium chloride and a few drops of dilute hydrochloric acid are added to a mixture of 44 gms. (1 mol.) of acetaldehyde and 100 gms. (excess) of alcohol. The whole is allowed to stand with occasional shaking for 1 hour, when the lower aqueous layer which has separated is siphoned off. The upper layer is placed over other 15 gms. of anhydrous calcium chloride, and after standing for 5 hours with constant shaking the separated aqueous layer is again siphoned off, and the upper layer added to a third 15 gms. of calcium chloride. This operation is once more repeated after 12 hours' standing, and the last lot allowed to act for 24 hours. It is filtered off and the filtrate fractionally distilled. The fraction 102°—108° is collected separately. The fraction below 102° is again allowed to stand over calcium chloride for 24 hours, and again fractionated as before; if preferred the fractionation may be performed under reduced pressure.

$$CH_3.CHO + 2C_2H_5OH = CH_3CH(OC_2H_5)_2 + H_2O.$$

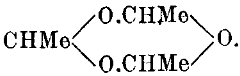
*Yield.*—60% theoretical (70 gms.). Colourless liquid; soluble in 18 volumes of water at 25°; miscible with alcohol; B.P. $^{760}$ 104°; D. $^{20}_{4}$ 0·831. (J., (1880), 694; B., 30, 3053; O. S., III., 1.)

The same compound may be obtained by dissolving 10 gms. of acetaldehyde in 50 gms. of a 1% absolute alcoholic solution of hydrogen chloride, and in 24 hours extracting the solution with ether after neutralisation with potassium carbonate. The extract is dried and purified by distillation as before.

**Reaction LXXXII. Condensation of an Aldehyde with itself under the Action of Mineral Acids or of Calcium Chloride.** (A., 27, 319; 162, 143; 203, 26, 43.)—If acetaldehyde is treated with calcium chloride or mineral acids, such as conc. sulphuric acid or gaseous hydrogen chloride, polymerisation occurs and paraldehyde is formed. A certain amount of metaldehyde is also obtained; its quantity increases with reduction in the temperature of polymerisation.



PREPARATION 152.—**Paracetaldehyde.**



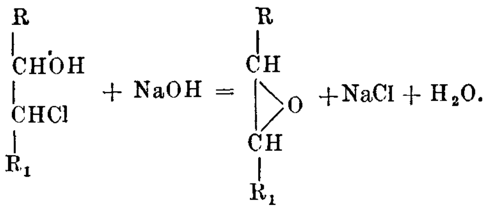
$C_6H_{12}O_3$. 132.

132 gms. (3 mols.) of freshly distilled *absolute* acetaldehyde are placed in a flask fitted with a thermometer, reflux condenser, and gas delivery tube, and the whole cooled to 5°. Dry hydrogen chloride is led in until an absorption of 6% (8 gms.) has taken place. The mixture is then allowed to stand for several hours at room temperature, and until the temperature has risen to the boiling point of acetaldehyde, 21°, when it is recooled to 5° and allowed to stand for 15 hours. Some metaldehyde has by then separated, and is filtered off. The liquid is shaken with a saturated solution of sodium carbonate to remove acid, and then washed with water. It is dried with anhydrous potassium carbonate and fractionated, the fraction 122°—128° being retained. The distillation can be carried out under reduced pressure.

$$3CH_3.CHO \rightarrow CH_3CH(OCH(CH_3))_2O.$$

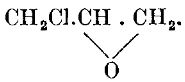
*Yield.*—70% theoretical (90 gms.). Colourless liquid; sparingly soluble in water; M.P. 12·5°; B.P. 124°; metaldehyde forms bright feathery crystals which readily sublime. (A., 27, 319; 162, 143; 203, 26, 43.)

**Reaction LXXXIII. Action of Caustic Alkali on the α β-chlorohydrins.** (A. Spl., (1861), 1, 221; J., 13, 456.)—When the chlorohydrins which contain chlorine and hydroxyl attached to adjacent carbons are heated with caustic alkali, elimination of hydrochloric acid occurs and an inner ether or oxide is obtained.



These oxides are unstable, reacting with water to form glycols, with hydrochloric acid to regenerate the chlorohydrin, and so on. The simplest member of this group, ethylene oxide, is especially unstable, it behaves almost as if it were unsaturated; it will even react with metallic chlorides to give the chlorohydrin.

PREPARATION 153.—**Epichlorohydrin.**



$C_3H_5OCl$. 92·5.

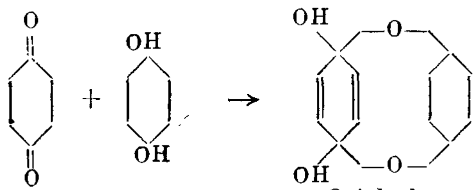
The dichlorohydrin (Preparation 317) is added to a slight excess of hot caustic soda (D. 1·5) solution contained in a distillation apparatus at reduced pressure, and is dropped in at approximately the same rate

as the epichlorohydrin distils over when the pressure is maintained below 100 mms. The distillate is separated, dried over anhydrous sodium sulphate, and systematically fractionated (p. 24). The fraction B.P. $^{760}$ 116°—117° is pure epichlorohydrin. Some dichlorohydrin is recovered.

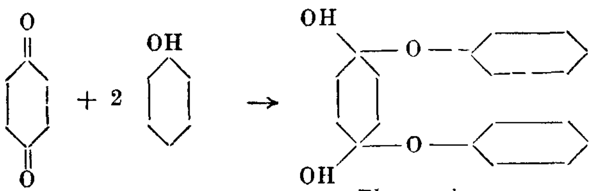
$$CH_2ClCH(OH).CH_2Cl + NaOH = \underbrace{CH_2.CH}_{O}.CH_2Cl + NaCl + H_2O.$$

*Yield.*—90% theoretical. Colourless mobile liquid; ethereal smell; B.P. 117°; D. $^0_4$ 1·203. (O. S., III., 47; J. S. C. I., C. and I., 49, 102.)

**Reaction LXXXIV. Addition of Phenols to Quinones.** (A., 200, 251; 215, 134; B., 24, 1341.)—Quinones readily react with 1 mol. of *p*-di-hydric phenols and 2 mols. of other phenols to form the highly coloured ether compounds, quinhydrones and phenoquinones respectively.



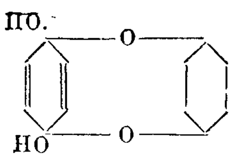

Quinhydrone.




Phenoquinone.

Quinhydrone can be prepared from quinone or quinol by partial reduction or oxidation respectively (see Preparation 154).

PREPARATION 154.—**Quinhydrone.**




$C_{12}H_{10}O_4$. 218.

*Method I.*—10 gms. (1 mol.) of quinone and 10 gms. (1 mol.) of quinol are separately dissolved in the minimum quantity of water, and the solutions mixed and warmed. After cooling, the precipitate is filtered off and washed with water.

$$O:C_6H_4:O + C_6H_4(OH)_2[1:4] = 1:4(OH)_2C_6H_4\overset{[1]\,O}{\underset{[4]\,O}{<>}}C_6H_4[1:4].$$

*Yield.*—Almost theoretical (20 gms.).

*Method II.*—10 gms. (1 mol.) of quinol are dissolved in water and heated

with an aqueous solution of 14·5 gms. (2 mols.) of ferric chloride. The quinhydrone rapidly separates. It is filtered off and washed with water.

$$C_6H_4(OH)_2 + 2FeCl_3 = C_6H_4O_2 + 2FeCl_2 + 2HCl.$$
$$C_6H_4O_2 + C_6H_4(OH)_2 = (OH)_2C_6H_4.O_2.C_6H_4.$$

*Yield.*—Almost theoretical (10 gms.). Lustrous green prisms or leaflets; quinone-like odour; soluble in warm petroleum ether; insoluble in cold water; M.P. 171°. (B., 24, 1341; 28, 1615.)

PREPARATION 155.—**Phenoquinone.**

$$\begin{matrix} C_6H_5O \diagdown & & \diagup OC_6H_5 \\ & C_6H_4 & \\ HO \diagup & & \diagdown OH. \end{matrix} \qquad C_{18}H_{16}O_4. \qquad 296.$$

20 gms. (1 mol.) of phenol and 12 gms. (1 mol.) of quinone are dissolved in petroleum ether or benzene and refluxed for 10 minutes. The solution is then concentrated on a water bath until crystals separate on cooling. They are filtered off and washed in water.

$$2C_6H_5OH + C_6H_4O_2 = (C_6H_5O)_2(OH)_2C_6H_4.$$

*Yield.*—Almost theoretical (32 gms.). Red acicular crystals; insoluble in water; somewhat soluble in warm petroleum ether; M.P. 71°; sublimes on heating. (A., 204, 251; 215, 134.)

The above preparation can also be performed in aqueous solution.

Resorcinolquinone and pyrogallolquinone are similarly prepared; they decompose at 90° and above 120° respectively.

# CHAPTER XV

## OXYGEN TO CARBON

## Oxy Compounds

### Aldehydes, Ketones, and Quinones

ALDEHYDES, ketones and quinones are important; most of the methods of preparing them come into this section. The reactions on which these methods are based are chiefly of two kinds—purely oxidising reactions (Preparation 440), and reactions involving hydrolysis followed by oxidation (Preparation 156).

**Reaction LXXXV. Simultaneous Oxidation and Hydrolysis of Monohalogen Compounds.** (A., 22, 1; 143, 186.)—When benzyl chloride or one of its derivatives is heated with an aqueous solution of a mild oxidising agent, such as copper nitrate, lead nitrate, etc., combined hydrolysis and oxidation occurs, and benzaldehyde or one of its derivatives is obtained.

$$C_6H_5CH_2Cl \xrightarrow{H_2O} C_6H_5CH_2OH \xrightarrow{O} C_6H_5CHO.$$

PREPARATION 156.—**Benzaldehyde** [*Phenyl-methanal*].

$$C_6H_5CHO. \qquad C_7H_6O. \qquad 106.$$

50 gms. (1 mol.) of benzyl chloride (see p. 349), 50 gms. (excess) of copper nitrate and 300 c.cs. of water are refluxed together in a current of carbon dioxide for about 8 hours, and until a sample of the oil present contains very little chlorine (test). The mixture is extracted with ether, the ether removed on a water bath, and the residual oil mechanically shaken for 1 hour with a saturated solution of sodium bi-sulphite. After standing for 2 hours, the crystals which have separated are filtered at the pump and washed first with a little alcohol and then with ether. They are warmed with excess of 10% sulphuric acid; the aldehyde which separates is extracted with ether, the extract dried over anhydrous sodium sulphate, the ether removed on a water bath and the residue distilled in a current of carbon dioxide. The fraction 176°—181° is retained.

$$2C_6H_5CH_2Cl + Cu(NO_3)_2 = 2C_6H_5CHO + CuCl_2 + 2HNO_2.$$

*Yield.*—40% theoretical (17 gms.). Colourless oil; characteristic odour; B.P. 179°; D. $^{15}_{4}$ 1·0504. (A., 22, 1; 143, 186.)

**Reaction LXXXVI. Hydrolysis of certain Dihalogen Compounds.** (A. Spl., 2, 253; A., 139, 319; D.R.P., 82927; 85493.)—When dihalogen compounds containing two halogen atoms attached to the one carbon

atom are boiled with water in presence of an alkali or certain metals, hydrolysis occurs, and an aldehyde or ketone is obtained.

$$R.CCl_2R_1 \xrightarrow{2H_2O} R.C(OH)_2R_1 \longrightarrow RCOR_1.$$

The process is used on a commercial scale to prepare benzaldehyde by heating benzal chloride with an aqueous suspension of chalk or milk of lime under pressure. Water is sufficient to bring about hydrolysis, the alkali is added to remove the hydrogen chloride formed, and so prevent the reverse reaction taking place. In place of an alkali, a trace of iron powder can be used; the reaction here takes a slightly different course, only 1 mol. of water being required for 1 mol. of the dichloride.

PREPARATION 157.—**Benzaldehyde** [*Phenyl-methanal*].

$$C_6H_5CHO. \qquad C_7H_6O. \qquad 106.$$

*Method I.*—20 gms. (1 mol.) of benzal chloride (see p. 350) are refluxed for 4 hours in an atmosphere of carbon dioxide with 200 c.cs. of water and 40 gms. of precipitated chalk in a round flask heated on an oil bath which is kept at 130°. The whole is then steam distilled in an atmosphere of carbon dioxide (see p. 24). The distillate is extracted with ether, the ether removed on a water bath and the residual benzaldehyde purified by means of its bisulphite compound, as described in Preparation 156.

$$C_6H_5CHCl_2 \xrightarrow{H_2O} C_6H_5CH(OH)_2 \longrightarrow C_6H_5CHO.$$

*Yield.*—70% theoretical (9 gms.). (A. Spl., 2, 253; 139, 319.)

*Method II.*—150 gms. (1 mol.) of benzal chloride (see p. 350) are heated in a round-bottomed flask to 30° with agitation; 0·5 gms. of iron powder and 25 gms. (excess) of water are then added, and the mixture cautiously heated until hydrogen chloride is evolved (about 100°). Heating may be discontinued until the action subsides, when more heat is applied. About 20 gms. sodium carbonate are added to give an alkaline reaction, and the benzaldehyde distilled in steam in an atmosphere of carbon dioxide and purified as described in Preparation 156.

$$C_6H_5CHCl_2 + H_2O \rightarrow C_6H_5CHO + 2HCl.$$

*Yield.*—80% theoretical (75 gms.). Colourless oil; characteristic odour; insoluble in water; soluble in ether; B.P. 179°; D. $^{15}_{4}$ 1·0504. (D.R.P., 82927; 85493.)

In all these preparations of benzaldehyde the chief loss is due to oxidation of the aldehyde to benzoic acid. The acid may be removed from the reaction mixture from which the benzaldehyde has been steam distilled by filtration while still hot, and acidification with much concentrated hydrochloric acid. Benzoic acid separates on cooling.

**Reaction LXXXVII. Hydrolysis of certain Anils.** (B., 35, 1228; D.R.P., 121745.)—When derivatives of toluene which contain negative groups in the *o*- and *p*-positions are treated with *p*-nitrosodimethyl-

aniline, owing to the activation of the methyl group by the presence of the two negative groups, condensation to an anil occurs.

$$C_6H_3(NO_2)_2(CH_3)[2:4:1] + C_6H_4(NO).N(CH_3)_2[1:4]$$
$$= C_6H_3(NO_2)_2CH : N.C_6H_4N(CH_3)_2 + H_2O.$$

These anils are readily hydrolysed by acids to yield derivatives of benzaldehyde.

$$C_6H_3(NO_2)_2CH : N.C_6H_4N(CH_3)_2 \xrightarrow{H_2O}$$
$$C_6H_3(NO_2)_2CHO + H_2N.C_6H_4N(CH_3)_2.$$

PREPARATION 158.—**2 : 4-Dinitrobenzaldehyde.**

$C_6H_3(NO_2)_2(CHO)[2:4:1]$. $C_7H_4O_5N_2$. 196.

50 gms. (1 mol.) of 2 : 4-dinitrotoluene, 50 gms. (excess) of *p*-nitroso dimethylaniline and 90 gms. of crystallised sodium carbonate are refluxed on a water bath for 6 hours with 300 c.cs. of alcohol. The anil which separates is filtered off, washed with boiling water, and recrystallised from acetone. The whole is then mechanically shaken for 4 hours with 350 gms. (excess) of nitric acid (D. 1·17) and 300 c.cs. of benzene, filtered, the benzene layer separated and the solvent removed on a water bath. The residue is recrystallised from alcohol, with the addition of animal charcoal, being precipitated from the alcoholic solution by dilution with water. The crystals which separate contain 1 mol. of alcohol of crystallisation; this they lose at 90°. The aqueous layer above is re-shaken with benzene and nitric acid, and worked up for further aldehyde as above.

$$C_6H_3(NO_2)_2(CH_3)[2:4:1] + NOC_6H_4N(CH_3)_2[1:4]$$
$$\rightarrow C_6H_3(NO_2)_2CH : NC_6H_4N(CH_3)_2 \xrightarrow{H_2O}$$
$$C_6H_3(NO_2)_2CHO[2:4:1] + H_2NC_6H_4N(CH_3)_2.$$

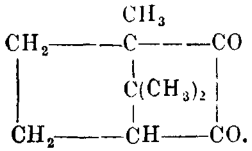
*Yield.*—80% theoretical (42 gms.). Yellowish crystals; insoluble in water; soluble in alcohol and benzene; M.P. 72°; B.P. $^{10}$ 190°; B.P. $^{20}$ 210°. (B., 35, 1228; D.R.P., 121745.)

**Reaction LXXXVIII. Action of Nitrous Acid on the Monoximes of α-Diketones.** (A., 274, 71.)—When compounds containing the group —$CH_2$—CO—are treated with nitrous acid in presence of sodium, an "*iso*-nitroso compound" identical with the monoxime of the corresponding α-diketone is obtained (see p. 111). From the monoxime by the further action of nitrous acid in the presence of glacial acetic acid, the diketone itself is formed.

$$\begin{array}{l} —CH_2 \\ \quad| \\ —CO \end{array} \xrightarrow{HNO_2} \begin{array}{l} —C : NOH \\ \quad| \\ —CO \end{array} \xrightarrow{HNO_2} \begin{array}{l} —CO \\ \quad| \\ —CO. \end{array}$$

It may be noted that aldehydes and ketones can usually be obtained from the corresponding oximes, phenyl-hydrazones, semi-carbazones, etc., by hydrolysis with dilute mineral acids.

PREPARATION 159.—**Camphorquinone.**



$C_{10}H_{14}O_2$. 166.

To 20 gms. (1 mol.) of *iso*-nitroso-camphor (see p. 307) dissolved in 35 c.cs. of glacial acetic acid, 9 gms. (excess) of sodium nitrite in 20 c.cs. of water are slowly added with mechanical stirring. Initially the temperature must not be allowed to rise above 20°, but when the evolution of gas ceases, the mixture is heated until no more gas is evolved. When cool, the whole is poured into an excess of cold water, and the precipitate filtered off at the pump, well washed with cold water, and dried on a porous plate. It is then sublimed at 60° (see p. 31).

$$C_8H_{14}\left\langle\begin{array}{l}C:NOH\\ |\\ CO\end{array}\right. + HNO_2 = C_8H_{14}\left\langle\begin{array}{l}CO\\ |\\ CO\end{array}\right. + N_2O + H_2O.$$

*Yield.*—50% theoretical (9 gms.). Yellow needles; sweet odour; insoluble in water; sublimes when heated; M.P. 198°. (A., 274, 71.)

**Reaction LXXXIX. Hydrolysis of Nitriles to Amides.** (B., 18, 355.)—When nitriles are heated with acids or alkalis they are hydrolysed to the corresponding acids passing intermediately through the amides. It is possible only in a few instances (*e.g.*, oxamide) to stop the hydrolysis at this intermediate stage, unless alkaline hydrogen peroxide is employed, when the amide is obtained in almost theoretical yield. Both methods of hydrolysis are illustrated in the following preparations.

$$R.C:N \xrightarrow{H_2O} R.CO.NH_2.$$

PREPARATION 160.—**Oxamide** [*Diamide of ethan-diacid*].

$$\begin{array}{l}CONH_2.\\ |\\ CONH_2.\end{array} \qquad C_2H_4O_2N_2. \qquad 88.$$

(To be carried out in a *good* fume cupboard.)

25 gms. (1 mol.) of crystallised copper sulphate are dissolved in 75 c.cs. of water in a distilling flask heated on a water bath, and a warm solution of 13 gms. (2 mols.) of 98% potassium cyanide in 25 c.cs. of water is added (*caution! cyanogen is extremely poisonous*). The evolved cyanogen is led into 20 c.cs. of cold conc. hydrochloric acid. When all the cyanide has been added, the second equivalent of cyanogen is expelled by adding, in the same way, a solution of 16 gms. (1 mol.) of ferric chloride in 20 c.cs. of water. Oxamide separates out, provided the hydrochloric acid is kept quite cool. It is washed with water.

$$\begin{array}{l}CN\\ |\\ CN\end{array} + 2H_2O + \begin{array}{l}CO.NH_2.\\ |\\ CO.NH_2.\end{array}$$

*Yield.*—50% theoretical (4·5 gms.). White crystalline solid; partly sublimes on heating, but for the most part decomposes; sparingly soluble in water and in alcohols. (B., 18, 355.)

PREPARATION 161.—**Benzamide** [*Amide of phenylmethan acid*].

$$C_6H_5.CO.NH_2. \qquad C_7H_7ON. \qquad 121.$$

20 gms. (1 mol.) of benzonitrile are added to 300 c.cs. (excess) of 3% (10 volumes) aqueous hydrogen peroxide containing 5 c.cs. of 2N caustic soda. The mixture is warmed on a water bath to 40°, and then shaken in an uncorked bottle until the oil has completely disappeared. The precipitate which forms is filtered off at the pump, and recrystallised from alcohol or hot water.

$$2C_6H_5CN + 2H_2O_2 = 2C_6H_5CO.NH_2 + O_2.$$

*Yield.*—Theoretical (24 gms.). White crystalline powder; soluble in hot water; M.P. 128°. (B., 18, 355.) See also O. S., XIII., 94.

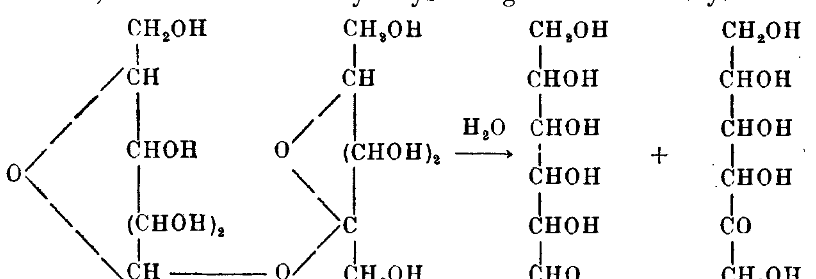
**Reaction XC. Hydrolysis of the Disaccharides.** (J. pr., [2] 2, 1, 245; B., 13, 1761; 28, 1429.)—When the disaccharides, and in fact all the glucosides, are heated with mineral acids, they are hydrolysed into their component monosaccharides or into their component monosaccharides and alcohols.

In this way

cane sugar yields glucose and fructose,
lactose yields glucose and galactose,
maltose yields glucose,
methyl glucoside yields glucose and methyl alcohol.

These hydrolyses can also be brought about by means of various enzymes, *e.g.*, invertase will hydrolyse cane sugar, maltase maltose, and so on. (See Haworth, "The Constitution of Sugars" (Arnold & Co., 1929).)

More complicated compounds can be brought within the scope of the reaction; thus starch can be hydrolysed to glucose in this way.



Cane sugar. Glucose. Fructose.

PREPARATION 162.—**Glucose** (*Pentolhexanal*, + − + +).

CHO
H.ĊOH
HOĊ.H $\qquad C_6H_{12}O_6. \qquad 180.$
H.Ċ.OH
H.Ċ.OH
ĊH₂OH.

70 gms. of fuming hydrochloric acid (38%) are mixed with 1,500 c.cs. of 95% alcohol, and the whole warmed on a water bath; 500 gms. of finely powdered cane sugar are gradually added with mechanical stirring, the temperature being kept at 50° throughout. When all the sugar has dissolved, the liquid is filtered, cooled, seeded with 0·5 gm. of glucose crystals, and allowed to stand for a week at ordinary temperature. The crystals which separate are filtered off at the pump, washed with absolute alcohol, and recrystallised by dissolving in a very little hot water to form a syrup, and adding hot methyl or ethyl alcohol until the solution becomes turbid. On cooling, the sugar which separates is filtered off at the pump, and washed with absolute alcohol.

$$\underset{\text{Cane sugar.}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Glucose.}}{C_6H_{12}O_6} + \underset{\text{Fructose.}}{C_6H_{12}O_6}.$$

Colourless crystals; very soluble in water; sparingly soluble in alcohol; M.P. 86° ($\cdot 1H_2O$); 146° (anhydrous). (J. pr., [2], 21, 245.)

**Reaction XCI.** (*a*) **Oxidation of Aromatic Hydrocarbons to Aldehydes by the action of Chromyl Chloride in Carbon Disulphide Solution.** (Etard.) (A. Ch., [5], 22, 225.)—In this reaction the hydrocarbon and chromyl-chloride are both dissolved in carbon disulphide, and the solutions carefully mixed. An explosive intermediate compound is precipitated, and this is separated and decomposed with water to give the aldehyde. The yields are very good, but the method is not often used owing to the inconvenience of working with carbon disulphide and the dangerous nature of the intermediate compounds.

$$RCH_3 + 2CrO_2Cl_2 = RCH.(OCr.Cl_2OH)_2.$$
$$R.CH.(OCrCl_2OH)_2 + 3H_2O = RCHO + 2CrO(OH)_2 + 4HCl.$$

PREPARATION 163.—**Benzaldehyde** [*Phenyl-methanal*].

$$C_6H_5.CHO. \qquad C_7H_6O. \qquad 106.$$

(*Great caution must be observed in performing this experiment. No flame must be brought near the apparatus.*)

10 gms. (excess) of toluene and 30 gms. (2 mols.) of chromyl chloride (see p. 513) are each dissolved in anhydrous carbon disulphide, the former in 50 gms., and the latter in 120 gms.; the former solution is placed in a litre flask fitted with a thermometer and long reflux condenser, and the latter is added in 10 c.cs. quantities, the reaction each time being allowed to moderate before further addition. Should no reaction occur on the first addition, the mixture is allowed to stand for 15 minutes before further addition. The reaction is very vigorous, and the flask must be cooled by immersing in a bath of ice-water, so that the temperature of the mixture never rises above 45°. When addition is complete, the mixture is allowed to stand for 3 hours, the explosive intermediate compound which appears as a precipitate is filtered off at the pump, well washed with anhydrous carbon disulphide, dried by blowing air through it, and decomposed by adding in small quantities to 1 litre of cold water. The chromic acid formed is reduced with gaseous sulphur dioxide, and the liquid steam

distilled in a current of carbon dioxide to remove benzaldehyde, which is extracted from the distillate with ether. The extract is dried over calcium chloride, the ether removed on a water bath, and the residue distilled in a current of carbon dioxide, the fraction 177°—182° being retained. (For the purification of the aldehyde by means of its bisulphite compound, see p. 226.)

Colourless oil; pleasant odour; insoluble in water; B.P. 179°; D. $^{15}_{4}$ 1·0504. (J. C. S., 91, 261.)

Benzaldehyde may be prepared from benzene by the direct action of carbon monoxide, see J. Eng., 25, 495.

**Reaction XCI.** (*b*) **Oxidation of Aromatic Hydrocarbons to Aldehydes by the action of Chromic Acid in Acetic Anhydride Solution.** (A., 311, 353; D.R.P., 121788.)—In the ordinary way, chromic acid oxidises hydrocarbons to aldehydes and then to acids. But if acetic anhydride and conc. sulphuric acid is present, the di-acetyl derivative of the aldehyde is formed and this does not undergo further oxidation. The aldehyde is obtained from the di-ester by hydrolysis. (*Cf.* the preparation of salicylaldehyde, p. 105.)

$$RCH_3 \xrightarrow{O_2} RCHO \xrightarrow{(CH_3CO)_2O} R.CH.(OCOCH_3)_2 \xrightarrow{HCl} R.CHO.$$

PREPARATION 164.—*Iso*-**Phthalaldehyde** (*m-Phthalaldehyde*).

$C_6H_4(CHO)_2[1:3]$. $C_8H_6O_2$. 134.

60 gms. (excess) of chromic acid are slowly added, with good agitation and cooling in a freezing mixture, to 15 gms. (1 mol.) of *m*-xylene mixed with 250 gms. glacial acetic acid, 500 gms. (excess) acetic anhydride, and 10 c.cs. conc. sulphuric acid. When all has been added, the mixture is kept at 0° until a sample gives a bulky white precipitate when shaken with cold water to decompose the anhydride. It is then poured on to powdered ice and stirred, until the oil formed solidifies. The *iso*-phthalaldehyde tetracetate is filtered off and recrystallised from methyl alcohol (M.P. 101°). The crystallised product is now heated under a reflux for 15 minutes with 150 c.cs. of 5% hydrochloric acid. On cooling, the aldehyde separates, is filtered and recrystallised from hot water.

$$C_6H_4(CH_3)_2 \longrightarrow C_6H_4[CH(OCOCH_3)_2]_2 \longrightarrow C_6H_4(CHO)_2.$$

*Yield.*—80% theoretical (15 gms.). Colourless needles; soluble in hot water; M.P. 89°. (A., 311, 353; D.R.P., 121788.)

**Reaction XCI.** (*c*) **Oxidation of Aromatic Hydrocarbons to Aldehydes by the Action of Cerium Dioxide in presence of Concentrated Sulphuric Acid.** (D.R.P., 158609.)—Cerium dioxide has the property of oxidising aromatic hydrocarbons to aldehydes and no further. The addition of a reagent to combine with the aldehyde group as formed is unnecessary.

$$RCH_3 \xrightarrow{CeO_2} R.CHO.$$

PREPARATION 165.—**Benzaldehyde** [*Phenyl-methanal*].

$C_6H_5CHO$. $C_7H_6O$. 106.

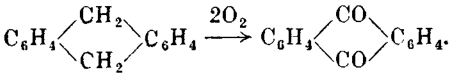
30 gms. (1 mol.) of toluene are heated to 60° with 1,500 gms. (excess) of sulphuric acid (D. 1·5) in a 2-litre round-bottomed flask fitted with a reflux condenser and mechanical stirrer (see Fig. 37). 250 gms. (excess) of cerium dioxide are gradually added, and the temperature allowed to rise to 90°. When no more dioxide remains, the whole is steam distilled until no more benzaldehyde passes over. Benzaldehyde is then recovered from the distillate as in Preparation 163.

$$C_6H_5CH_3 + O_2 = C_6H_5CHO + H_2O.$$

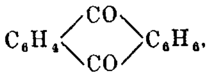
*Yield.*—70% theoretical (25 gms.). See p. 232. (D.R.P., 158609; J. S. C. I., 51, 159.)

**Reaction XCII.** (*a*) **Action of Oxidising Agents on Methylene Groups in Aromatic Compounds.** (B., 6, 1347; A. Spl., (1869), 7, 284; A., 279, 258.)—When compounds containing methylene groups attached to two aromatic residues are heated with oxidising agents—chromic acid is usually employed—the two hydrogens of each methylene group are replaced by oxygen to yield carbonyl compounds, which have some or all of the properties of ketones and of quinones.

It is to be noted that ethylene itself can be converted to glycol in presence of selenium dioxide. (E.P., 376306.)



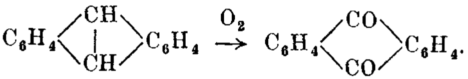
Preparation 166.—**Anthraquinone.**



$C_{14}H_8O_2$. 208.

Anthracene is sublimed with superheated steam (see p. 25) at 200°. This reduces it to a fine state of division.

100 gms. (1 mol.) of moist sublimed anthracene are stirred up with 2 litres of water in a lead-lined pot, fitted with a glass agitator; 200 gms. (excess) of sodium dichromate are added at the same time. The mixture is heated to 80° and 600 gms. (excess) of 50% sulphuric acid are added from a dropping funnel during 10 hours. The presence of chromic acid must always be clearly shown (test with hydrogen peroxide). The mixture is then boiled for 2 hours, evaporated water being replaced at intervals. The product is filtered off, thoroughly washed and dried. It is heated in $2\frac{1}{2}$ times its weight of conc. sulphuric acid at 120° as long as $SO_2$ is evolved. After 3 hours it is poured into 3 times its weight of water, and the anthraquinone, which is precipitated, filtered off at the pump. It may be further purified by sublimation at 250°.

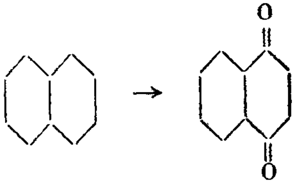


*Yield.*—90% theoretical (105 gms.). Yellow needles; insoluble in water; soluble in glacial acetic acid; sublimes on heating at 250°;

M.P. 277°; B.P. 382°; is an important intermediate in the preparation of vat dyestuffs. (B., 6, 1347; A. Spl., 1869, 7, 284.)

Anthraquinone does not possess the properties of a true quinone.

**Reaction XCII.** (*b*) **Oxidation of Aromatic Hydrocarbons to Quinones.** (J. C. S., 37, 634; A., 167, 139, 357.)—Although benzene does not react in this way polynuclear aromatic hydrocarbons can be oxidised directly to give quinones analogous to both *o*- and *p*-quinones. The oxidising agent used is chromic acid in glacial acetic acid. The amino-compounds, however, give better yields (see Reaction XCIII.).



PREPARATION 167.—**α-Naphthaquinone.**

$C_{10}H_6O_2$. **158.**

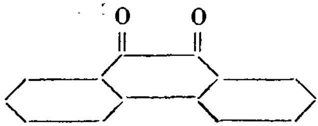
10 gms. (1 mol.) of naphthalene dissolved in 100 c.cs. glacial acetic acid are gradually added with good agitation to 10 gms. (excess) of chromic acid dissolved in 70 c.cs. of 80% acetic acid, the whole being kept at 0°. After standing for 4 days at the ordinary temperature with occasional shaking, the liquid is poured into a litre of water. The precipitated naphthaquinone is then filtered, washed with water and recrystallised from alcohol.

$$C_{10}H_8 + 3O \rightarrow C_{10}H_6O_2 + H_2O.$$

*Yield.*—40% theoretical (5 gms.) (*cf.* yield in Preparation 171). Yellow plates with sharp odour; insoluble in water; soluble in hot alcohol; volatile in steam; M.P. 125°. (J. C. S., 37, 634; A., 167, 357.)

(*Cf.* *p*-benzoquinone, p. 235.)

PREPARATION 168.—**Phenanthraquinone.**



$C_{14}H_8O_2$. **208.**

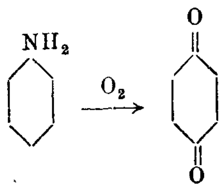
30 gms. (1 mol.) of phenanthrene are dissolved in 150 gms. of warm glacial acetic acid, and 80 gms. (excess) of chromic acid dissolved in about 250 gms. of glacial acetic acid are gradually added. This latter solution is prepared by dissolving the chromic acid in the *minimum* quantity of water, and pouring into glacial acetic acid. The addition is regulated

so that the heat of reaction keeps the mixture just on the boil throughout. When addition is complete most of the acetic acid is distilled off, and the residue treated with much water. The precipitate is filtered at the pump, washed with a little hot water, shaken with a warm dilute sodium bisulphite solution and filtered ; the filtrate is warmed on a water bath, and the quinone precipitated by addition of sulphuric acid. This precipitate is recrystallised from an excess of boiling alcohol.

$$C_{14}H_{10} + 3O = C_{14}H_8O_2 + H_2O.$$

*Yield.*—Almost theoretical (35 gms.). Orange needles ; odourless ; not volatile in steam ; insoluble in water and in cold alcohol ; soluble in glacial acetic acid ; M.P. 198°. (A., 167, 139.)

**Reaction XCIII. Oxidation of Primary Aromatic Amines and their** ***para*-substituted Derivatives to Quinones.** (A., 27, 268 ; 194, 202 ; 211, 49 ; 215, 125 ; B., 19, 1467 ; 20, 2283 ; 25, 982 ; 36, 4390.)—Many primary aromatic amines, when oxidised with chromic acid, readily yield *p*-quinones, aniline, for example, giving *p*-benzoquinone.



The mechanism of this reaction is not simple, but is probably as follows :

$$C_6H_5NH_2 \rightarrow C_6H_5\overset{H_2}{N} = O \rightarrow C_6H_5NHOH$$

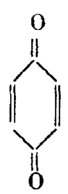
Aniline. Phenyl-ammoninm oxide. Phenyl-hydroxylamine.

$$\rightarrow NH_2,C_6H_4.OH \rightarrow O : C_6H_4 : O.$$

*p*-Aminophenol (see Prep. 139.) Benzoquinone.

In support of this view the *p*-amino-phenols themselves readily yield quinones. Also most *p*-substituted primary amines, *e.g.*, *p*-diamines, *p*-alkylamines, such as *p*-toluidine, sulphanilic acid and its derivatives, behave similarly. In fact, the reaction can be used as a test for *p*-substituted primary amines. *p*-Benzoquinone is usually made from aniline ; for the other *p*-quinones the *p*-amino-phenols, which are easily obtained by reduction of the *p*-nitroso-phenols and of azo-phenols, are employed. These reactions also apply, but not so widely, in the naphthalene series.

PREPARATION 169.—*p*-**Benzoquinone** (*Quinone*).



$C_6H_4O_2$. 108.

To 50 gms. (1 mol.) of aniline dissolved in 1,300 gms. (excess) of 25% sulphuric acid a cold 20% solution of 50 gms. of sodium dichromate is slowly added in 3 hours, with good cooling and mechanical stirring. The temperature must throughout be kept below 4°. When all the dichromate has been dropped in the whole is allowed to stand for 24 hours, and 100 gms. of sodium dichromate added in the same manner as before. After 6 hours the liquid is extracted 6 times with its own volume of ether, the latter being recovered each time by distillation and used again. The shaking must not be too vigorous as the mixture tends to emulsify very readily. The crude product from the ether extraction is distilled in steam (see p. 24).

If sodium dichromate is not available the potassium salt may be employed. The same quantities are taken as with the sodium salt, but the potassium salt is added in the form of powder, and not in aqueous solution.

It is usual to treat half of the solution, after oxidation is complete, with sulphur dioxide to obtain quinol (see p. 187). As quinone is more difficult to extract with ether from water than quinol, the whole resulting solution may be worked up for quinol, and the latter, when purified, oxidised with sodium dichromate solution to quinone.

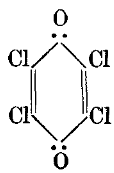
$$C_6H_5NH_2 \xrightarrow{O_2} O : C_6H_4 : O.$$

*Yield.*—70% theoretical (40 gms.). Yellow, acicular crystals; penetrating odour; slightly soluble in water; soluble in alcohol and ether; sublimes on heating; M.P. 116°. (A., 27, 268; 45, 354; 200, 240; 215, 125; B., 19, 1467; 20, 2283; O. S., VIII., 122.)

In an exactly similar way *o*-tolu-*p*-quinone (M.P. 67°) may be prepared from *o*-toluidine.

For electrolytic oxidation of benzene to *p*-benzoquinone and quinol, see E.P., 430572.

PREPARATION 170.—**Chloranil** (*Tetrachloro*-p-*benzoquinone*).



$C_6O_2Cl_4$. 246.

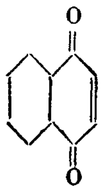
20 gms. (1 mol.) of 2 : 6-dichloro-4-nitroaniline are reduced to 2 : 6-dichloro-1 : 4-diaminobenzene by refluxing with 800 c.cs. (excess) of conc. hydrochloric acid and 30 gms. (excess) of tin. While still hot, 20 gms. (excess) of potassium chlorate are gradually added, the liquid being maintained at the boil for 15 minutes after all the chlorate has been added. The liquid is diluted with much water and filtered; the precipitate is well washed with water, dried, and recrystallised from boiling toluene.

$$C_6H_2Cl_2(NH_2)_2[2: 6 : 1 : 4] \xrightarrow{O_2 + Cl_2} C_6Cl_4O_2.$$

*Yield.*—90% theoretical (22 gms.). Yellow leaflets; characteristic odour; insoluble in water; sublimes on heating. (B., 36, 4390.)

The potassium chlorate both oxidises and chlorinates. If chromic acid, or even weaker oxidising agents, is employed the dichloro-quinone is obtained. The oxidation of aminophenols is illustrated in the following, in which nitrous acid serves as oxidising agent.

PREPARATION 171.—α-**Naphthaquinone.**



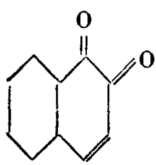
$C_{10}H_6O_2$. 158.

To 20 gms. of finely powdered 1 : 4-aminonaphthol, or an equivalent amount of one of its salts suspended in 100 c.cs. (excess) of hydrochloric acid (D. 1·05), 20 gms. (excess) of sodium nitrite are slowly added. The precipitate formed is well washed with water, filtered, and dried on a porous plate. The filtrate is extracted with ether, the extract dried over calcium chloride, filtered, and the ether removed on a water bath at 60°. The residue and the dried precipitate are recrystallised from petroleum ether.

$$C_{10}H_6(OH)(NH_2)[1:4] \xrightarrow{O_2} C_{10}H_6O_2[1:4].$$

*Yield.*—80% theoretical (16 gms.). Yellowish plates; characteristic odour; soluble in hot alcohol; volatile in steam; sublimes at 100°; M.P. 125°. (A., 183, 242.)

PREPARATION 172.—β-**Naphthaquinone.**



$C_{10}H_6O_2$. 158.

50 gms. (1 mol.) of finely powdered 1 : 2-aminonaphthol (see p. 365) are suspended in 250 c.cs. of 30% sulphuric acid, and 30 gms. (excess) of 10% aqueous potassium or sodium dichromate solution slowly added with mechanical stirring, the temperature being maintained at 0°. The precipitate is filtered off, well washed with water, dried on a porous plate, and recrystallised from petroleum ether.

$$C_{10}H_6(OH)(NH_2)[1:2] \rightarrow C_{10}H_6O_2[1:2].$$

*Yield.*—75% theoretical (35 gms.). Red acicular crystals; odourless; non-volatile in steam; M.P. 115°. (A., 189, 153; 194, 202; 211, 49; B., 25, 982.)

The preparations of α- and β-naphthaquinone should be compared with

those of phenanthraquinone, and the corresponding benzoquinones (see p. 235).

**Reaction XCIV. Conversion of Nitriles to Aldehydes by the Action of Hydrochloric Acid and Stannous Chloride followed by Hydrolysis of the Aldime-Stannichloride so formed** (Stephen). (J. C. S., 127, 1874.)—When a nitrile is added to anhydrous stannous chloride (p. 507) in dry ether saturated with hydrogen chloride, a white crystalline aldime-stannichloride separates, owing to the reduction of the imino-chloride first formed :

$$R.C \vdots N + HCl \rightarrow R.CCl : NH.$$
$$R.CCl : NH + SnCl_2 + 2HCl \rightarrow R.CH : NH.HCl + SnCl_4.$$

Two hours is usually sufficient time for the completion of the reaction and the separation of these salts. The products are readily hydrolysed by warm water. The yields from aliphatic and aromatic (other than *o*-substituted) nitriles are usually quantitative. The method has found an important application in the synthesis of thyroxine (Ann. Rep., 1926, 236.) The details of the following preparation constitute a general method of procedure.

PREPARATION 173.—**Octaldehyde.**

$$CH_3(CH_2)_6CHO. \qquad C_8H_{16}O. \qquad 128.$$

57 gms. of finely powdered, anhydrous stannous chloride (1·5 mols.) are suspended in 200 c.cs. dry ether, which is then saturated with dry hydrogen chloride until the mixture separates into two layers, the lower viscous layer consisting of stannous chloride dissolved in ethereal hydrogen chloride. 25 gms. of octonitrile are now added with vigorous shaking. After a few minutes, separation begins of the white crystalline aldime-stannichloride, which is collected after two hours, and the aldehyde liberated by distillation in steam (p. 24).

Colourless oil; lemon-like odour; B.P. $^{11}$ 65°.

# CHAPTER XVI

## OXYGEN TO CARBON

## Hydroxy-Oxy Compounds

### Acids

Various hydrolytic and oxidation reactions give rise to acids—the hydroxy-oxy compounds which have the hydroxy and oxy (carbonyl) groups attached to the one carbon. In none of the reactions is the product of necessity a hydroxy-oxy compound with these groups attached to different carbons.

**Reaction XCV. Hydrolysis of Nitriles.** (B., 19, 1950; 20, 241, 592; A., 258, 10.)—On heating with aqueous solutions of mineral acids or alkalis, the nitriles are converted respectively into the corresponding acids or into the alkali salts of the latter. Aqueous solutions of sodium carbonate can also be employed if the heating is performed under pressure. The reaction occurs in two stages.

$$RC\vdots N \xrightarrow{H_2O} R.CO.NH_2 \xrightarrow{HOH} R.COOH.$$

It is difficult to stop the hydrolysis at the intermediate amide stage (see p. 229).

It is not always necessary to isolate the nitriles on their formation in order to hydrolyse them to acids (see p. 158). Also without isolation, the acid formed can be simultaneously esterified by using for hydrolysis aqueous alcoholic solutions of sulphuric acid (see p. 256; *cf.* also p. 257).

In all these reactions water is the hydrolysing agent, the acid or alkali acting merely as catalyst.

Preparation 174.—**Mandelic Acid** (*Phenylglycollic Acid*).

$$C_6H_5CH(OH)COOH. \qquad C_8H_8O_3. \qquad 152.$$

(*This preparation should be conducted in a fume cupboard.*)

65 gms. freshly prepared mandelonitrile (p. 156) and 85 c.cs. conc. hydrochloric acid are placed in an evaporating basin and the mixture allowed to stand for 12 hours. It is then heated on a steam bath to remove excess water and hydrochloric acid. The mixture, after heating for 6 hours, is cooled, with stirring, and the mandelic acid and ammonium chloride which separate filtered off. The filtrate is evaporated to dryness. The total residue is dried in air and ground in a mortar. The mixture is then washed twice in a flask with 150 c.c. portions of cold benzene, and again filtered. The mandelic acid is separated by extracting in a Soxhlet apparatus with hot benzene and crystallising.

$$C_6H_5CH(OH)CN \longrightarrow C_6H_5CH(OH)COOH.$$

*Yield.*—60% theoretical (45 gms.). Rhombic crystals; M.P. 118°. (J. C. S., 113, 12; O. S., VI., 59.)

PREPARATION 175.—***p*-Toluic Acid** (1-*Methyl*-4-*carboxy-benzene*).

$$C_6H_4(CH_3)(COOH)[1:4]. \qquad C_8H_8O_2. \qquad 136.$$

20 gms. (1 mol.) of *p*-toluonitrile (see p. 154) are refluxed with 160 gms. (excess) of 85% sulphuric acid, until crystals appear in the condenser. The well-cooled mixture is diluted with two volumes of water, and the precipitate filtered, well washed with cold water, and recrystallised from hot water or aqueous alcohol with the addition of charcoal.

$$C_6H_4(CH_3)(CN)[1:4] \xrightarrow{H_2O} C_6H_4(CH_3)(COOH)[1:4].$$

*Yield.*—85% theoretical (20 gms.). Colourless crystals; soluble in hot water and in alcohol; M.P. 178°. (A., 258, 10.) See also J. Eng., 23, 1129.

PREPARATION 176.—**Phenylacetic Acid** [*Phenylethan acid*].

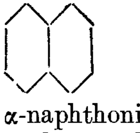
$$C_6H_5CH_2COOH. \qquad C_8H_8O_2. \qquad 136.$$

50 gms. (1 mol.) of benzyl cyanide and 150 gms. (excess) of 80% sulphuric acid are placed in a ½-litre round-bottomed flask connected by a glass tube bent twice at right angles with a second ½-litre round-bottomed flask fitted with a two-holed cork. The end of the tube is flush with the cork in one hole. Through the second hole passes a vertical glass tube, 50 cms. long, dipping just below the surface of 250 c.cs. of water in the flask. In the middle of this tube a large bulb is blown. The whole apparatus is fitted up in a fume cupboard. The mixture is gently heated by a naked flame, until small bubbles are seen to rise from the surface of the lower layer of acid. In a few minutes a vigorous reaction begins, the liquid in the flask boils, and a small quantity of benzyl cyanide distils over into the second flask, some of the water in which is forced up into the bulb. When the reaction is over, the flask is again heated for 3 minutes and allowed to cool, its contents solidifying in so doing. The solid residue is washed with cold water, dissolved in hot water, the solution neutralised with sodium carbonate, filtered hot, the filtrate acidified with dilute sulphuric acid, and allowed to stand. The crystals which separate are filtered off, washed with cold water, and recrystallised from hot water.

$$2C_6H_5CH_2.CN + 4H_2O + H_2SO_4 = 2C_6H_5CH_2COOH + (NH_4)_2SO_4.$$

*Yield.*—80% theoretical (46 gms.). Colourless thin laminated crystals; soluble in hot water; M.P. 76·5°; B.P. 262°; K = 0·0056. (B., 19, 1950; 20, 592; Bl., 37, 287; O. S., II., 63.)

PREPARATION 177.—**α-Naphthoic Acid** (1-*Carboxynaphthalene*).




$$C_{11}H_8O_2. \qquad 172.$$

15 gms. (1 mol.) of α-naphthonitrile, 10 gms. (excess) of caustic soda, and 75 c.cs. of 95% alcohol are heated in a sealed tube (see p. 41) at

170° for 5 hours. On opening, the contents of the tube are diluted with 5 volumes of water, and carefully acidified with conc. hydrochloric acid. The precipitate is filtered at the pump, washed with water, and recrystallised from alcohol.

$$C_{10}H_7CN + NaOH + H_2O = C_{10}H_7COONa + NH_3.$$

*Yield.*—90% theoretical (15 gms.). Colourless crystals; insoluble in water; soluble in alcohol; M.P. 160°. (B., 20, 241.) See also O. S., XI., 80.

**Reaction XCVI. Hydrolysis of Esters to Acids.** (A., 186, 161; 204, 127; 215, 26; Ann. Rep., 1930, 146.)—When esters are heated with water, hydrolysis occurs, but does not go to completion, the reaction being reversible.

$$R.CO.OR_1 + H_2O \rightleftarrows RCOOH + HOR_1.$$

If, however, aqueous or alcoholic caustic alkali is used, by combining with the acid as formed, it shifts the equilibrium point of the reaction, and almost complete hydrolysis occurs. This reaction could also have been dealt with under Chapter XIII, since alcohols are simultaneously formed; however, the hydrolysis is more usually undertaken to obtain the acid. Other special cases of hydrolysis have been dealt with elsewhere (see Reaction LXVII.). The general method of procedure will be clear from the following.

PREPARATION 178.—**Acetic Acid** [*Ethan-acid*].

$$CH_3.COOH. \qquad C_2H_4O_2. \qquad 60.$$

20 gms. (1 mol.) of ethyl acetate (see p. 256) are refluxed with 80 gms. (excess) of 25% aqueous caustic potash for 1 hour, until the layer of ester has disappeared, and the mixture no longer smells of it. The whole is then distilled to 100°; ethyl alcohol can be separated from the distillate by addition of anhydrous potassium carbonate. The residue in the flask is neutralised with dilute sulphuric acid and evaporated to dryness on a water bath. The solid residue is powdered and distilled with 50 gms. of conc. sulphuric acid to 130°, and the distillate fractionated between 115° and 120°.

Cooling in ice until solidification takes place, and subsequently draining away the still-liquid portion, gives crystals of glacial acetic acid.

*Yield.*—90% theoretical (12 gms.). Colourless liquid or crystals; characteristic odour; miscible with water; M.P. 16·7°; B.P. 119°; D. $^{15}_{4}$ 1·055. (Phil. Trans., 156, 37; Bl., 33, 350.)

PREPARATION 179.—**Ethylmalonic Acid** [*Ethylpropan diacid*].

$$C_2H_5.CH(COOH)_2. \qquad C_5H_8O_4. \qquad 132.$$

20 gms. of diethyl-ethylmalonate (see p. 137) are gradually added to 50 gms. (excess) of 50% aqueous caustic potash in a flask fitted with a reflux condenser, and cooled in water. The mixture so obtained is heated on a water bath with shaking until, after a vigorous reaction, complete liquefaction has occurred (1 hour). The liquid is cooled, diluted with an equal volume of water, acidified with conc. hydrochloric acid, and ex-

tracted with ether. The extract is dried over anhydrous sodium sulphate, filtered, the ether removed on a water bath, and the residue recrystallised from benzene.

The ethylmalonic acid can also be worked up by precipitating its calcium salt from the neutralised solution by addition of a concentrated solution of calcium chloride, and treating the solid salt with conc. hydrochloric acid, extracting the liberated acid with ether, and proceeding as above.

$$C_2H_5CH(COOC_2H_5)_2 + 2KOH = C_2H_5CH(COOK)_2 + 2C_2H_5OH.$$

*Yield.*—85% theoretical (12 gms.). Colourless prisms; soluble in water, alcohol and ether; M.P. 112°. (A., 204, 134.)

Like all the malonic acids, this acid loses carbon dioxide on heating, yielding butyric acid, B.P. 163°. The reaction is carried out by heating 10 gms. of the acid in a reflux apparatus to 180° until carbon dioxide is no longer evolved ($\frac{1}{2}$ hour). The residue is fractionated for butyric acid between 160° and 165°.

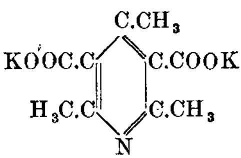
PREPARATION 180.—**Soap from Olive Oil.**

100 gms. of olive oil are heated in a beaker with 7 gms. of solid caustic soda and a little piece of soap in 75 c.cs. water for about 20 minutes. Another portion of 7 gms. caustic soda in 20 c.cs. of water is now added and heating continued for a further 20 minutes. Vigorous agitation should be maintained throughout the whole of this saponification, which should now be complete. A sample of the soap should be soluble in much water on heating; if not, a little more alkali solution should be added and heating continued, 100 gms. of common salt are added, stirred to dissolve, and the mixture allowed to cool. The cake which separates on the top is filtered and pressed (p. 33). Glycerine can be obtained from the filtrate by acidification, concentration, removal of the common salt, and vacuum distillation.

Olive oil is a mixture of glycerides, chiefly olein.

$$C_3H_5(O.COC_{17}H_{33})_3 + 3NaOH \longrightarrow C_3H_5(OH)_3 + 3NaOOC.C_{17}H_{33}.$$

PREPARATION 181.—**Potassium Collidine Dicarboxylate** (*Dipotassium-*2 : 4 : 6-*trimethyl-pyridine*-3 : 5-*dicarboxylate*).




$C_{10}H_9O_4NK_2$. 285.

10 gms. of diethyl-collidine dicarboxylate (p. 411) are refluxed on a water bath for 4 hours with about 10 times the volume (excess) of alcoholic potash (2·5 N approx.). The alcoholic solution is decanted from the separated potassium salt, a further yield of which is obtained by adding ether to the alcoholic solution. The total product is washed with alcohol, then with ether and dried.

$$C_5N(CH_3)_3(COOC_2H_5)_2 + 2KOH = C_5N(CH_3)_3(COOK)_2 + 2C_2H_5OH.$$

*Yield.*—Almost theoretical (11 gms.). White crystalline mass; insoluble in ether. (A., 215, 26.)

**Reaction XCVII. Hydrolysis of Amides, Acid Chlorides and Acid Anhydrides.** (A., 188, 73; B., 26, R., 773; 28, R., 917, 32, 1118.)—All these compounds on hydrolysis yield acids. The anhydrides are hydrolysed by treatment with water or dilute alkali, the acid chlorides are usually very rapidly hydrolysed by water, but in the aromatic series 10% caustic alkali is sometimes necessary. The amides are boiled with caustic alkali solution (10%) or with conc. hydrochloric or sulphuric acid. They are, especially the substituted aromatic amides, very resistant to the action of acids, so that the former method is the best. Another method is to dissolve the amide in conc. sulphuric acid, and add sodium nitrite in the cold, afterwards gently warming. Sometimes dilute sulphuric acid and addition of the nitrite in the warm gives better results.

$$C_6H_5CONH_2 + O : NOH = C_6H_5COOH + N_2 + H_2O.$$

PREPARATION 182.—**Citraconic Acid** [Cis-3-*carboxyl*-2-*buten acid*].

$$\begin{array}{l} CH_3 \\ | \\ C.COOH \\ \| \\ CH.COOH. \end{array} \qquad C_5H_6O_4. \qquad 130.$$

3·2 gms. (1 mol.) of water are added to 20 gms. (1 mol.) of citraconic anhydride (p. 414), and the mixture well stirred. The whole solidifies, on standing, to a mass of crystals which are dried on a porous plate.

$$\begin{array}{l} CH_3 \\ \cdot \\ C.CO \\ \| \quad \searrow O + H_2O \\ \| \quad\ \ | \\ CH.CO \end{array} = \begin{array}{l} CH_3 \\ \cdot \\ C.COOH \\ \| \\ \| \\ CH.COOH \end{array}$$

*Yield.*—Theoretical (23 gms.). Colourless crystals; soluble in ether and chloroform; very soluble in water; M.P. 85°; K = 0·340. (A., 188, 73.)

**Reaction XCVIII. Simultaneous Oxidation and Hydrolysis of Benzyl and Benzylidene Chlorides and their Derivatives.** (Bl., 7, 100; B., 10, 1275).—If benzyl or benzylidene chloride, or derivatives, are refluxed with an aqueous solution containing sodium carbonate and potassium permanganate, simultaneous hydrolysis and oxidation occurs, and benzoic acid or one of its derivatives is produced.

$$C_6H_5.CH_2.Cl \xrightarrow{Na_2CO_3} C_6H_5CH_2OH \xrightarrow{O_2} C_6H_5COOH.$$

$$C_6H_5.CH.Cl_2 \xrightarrow{Na_2CO_3} C_6H_5.CHO \xrightarrow{O_2} C_6H_5COOH.$$

PREPARATION 183.—**Benzoic Acid** [*Phenylmethan acid*].

$$C_6H_5COOH. \qquad C_7H_6O_2. \qquad 122.$$

To a mixture of 10 gms. (6 mols.) of benzyl chloride, 8 gms. (excess) of anhydrous sodium carbonate, and 15 c.cs. of water boiling under a reflux condenser, 17 gms. (8 mols.) of potassium permanganate in 250 c.cs. of water are added gradually, and the boiling continued until the colour of the permanganate has been discharged. Sulphur dioxide is then bubbled through the warm liquid until the precipitated manganese dioxide has dissolved. On cooling benzoic acid separates; it is filtered at the pump, washed with a little cold water, and recrystallised from hot water.

*Yield.*—Theoretical (9 gms.). Colourless needles; soluble in hot water, alcohol and ether; volatile in steam; M.P. 121°. (B., 10, 1275.)

**Reaction XCIX. Oxidation of certain Carbon Compounds to less complex Compounds.**—Complex compounds under vigorous oxidation yield simpler compounds, usually highly oxygenated. Such reactions are of value in determining the structure of certain compounds.

Oxalic is formed from the sugars, especially under the influence of $V_2O_5$, whereas in the presence of manganese salts tartaric acid is formed. (J. pr., 75, 146; U.S.P., 1,870,472.)

The preparation of maleic anhydride (U.S.P., 1,515,299) by the oxidation of benzene by oxygen in presence of $V_2O_5$ constitutes an important industrial development, the anhydride being converted into succinic acid by reduction with hydrogen and nickel (U.S.P., 1,491,465), and into malic acid by hydration.

PREPARATION 184.—**Oxalic Acid** [*Ethan diacid*].

$$(COOH)_2.2H_2O. \qquad C_2H_2O_4(+H_4O_2). \qquad 90(+36).$$

140 c.cs. (excess) of conc. nitric acid and 0·1 gm. of vanadium pentoxide are gently warmed in a 1-litre round-bottomed flask on a water bath. The flask is then removed to a fume cupboard, and 22 gms. (1 mol.) of cane sugar are added all at once. As soon as brown fumes are evolved in large quantities, the flask is placed in cold water, and allowed to stand 24 hours, when the crystals which have separated are filtered off. A further small quantity may be obtained by allowing the mother liquors to stand. The crystals are drained on a small porcelain funnel without filter paper, and recrystallised from a very small quantity of water.

$$C_{12}H_{22}O_{11} + 9O_2 = 6(COOH)_2 + 5H_2O.$$

*Yield.*—25% theoretical (8 gms.). Colourless needles; soluble in water and alcohol; sparingly soluble in ether; water of crystallisation given off at 100°—105°; M.P. 101·5°. K = 10. (J. pr., 75, 146.)

**Reaction C. Oxidation of the Side Chain in Aromatic Compounds.** (A., 122, 184; 133, 41; 137, 308; 141, 144; 147, 292; B., 7, 1057; 19, 705; Z. Ch., 4, 119) (Fittig).—When aromatic compounds containing aliphatic side chains attached to the nucleus are treated with certain oxidising agents (potassium permanganate, dilute nitric acid, and chromic acid), the side chain is oxidised until only a carboxylic group attached to the nucleus remains; the end methyl group, if there are several carbon atoms

present, being first oxidised to carboxyl and split off, and so on down to the first. If several side chains are present the results vary with the reagent and the orientation of the side chains. Thus, if there are two, dilute nitric acid and potassium permanganate oxidise only one side chain, while chromic acid oxidises both, unless they are in the *ortho*-position to one another, when the compound is either not attacked or destroyed. Somewhat the same applies to nuclear substituted benzenes with one side chain; the *ortho*-compound is often unattacked or destroyed, whereas the *para*- and *meta*-compounds yield the corresponding acids. Nitro groups in the *ortho*-position hinder oxidation; with halogen groups the *meta*-compound is least, and the *para* most readily attacked. The methods for the employment of the various reagents mentioned will be clear from the following preparations. Particular attention should be paid to the method of oxidation of the side chains in phenols and amines. Before such oxidation can be carried out these substituting groups must be protected, the phenol by forming its sulphuric or phosphoric acid ester, the amine by benzoylation or acetylation. For the protected amines, potassium permanganate in presence of magnesium sulphate is used; alkaline permanganate is the best oxidising agent for phenol esters.

PREPARATION 185.—**3 : 5-Dimethylbenzoic** (*Mesitylenic Acid*).

$C_6H_3.(CH_3)_2(COOH)[1:3:5]$. $C_9H_{10}O_2$. 150.

**1-Methyl-3 : 5-dicarboxybenzene** (*Uvitic Acid*).

$C_6H_3(CH_3)(COOH)_2(1:3:5)$. $C_9H_8O_4$. 180.

20 gms. (1 mol.) of mesitylene are refluxed with 80 gms. (excess) of 30% nitric acid in a 250-c.c. round-bottomed flask, on a sand bath in a fume cupboard for 18 hours. The white residue is filtered off on cooling, washed with cold water, dissolved in sodium carbonate solution, unattacked mesitylene and nitromesitylene separated, and the mixed acids reprecipitated by acidification with dilute hydrochloric acid. The white precipitate is filtered off, washed with cold water, and heated on a water bath with tin and excess of strong hydrochloric acid for 2 hours with constant shaking in a capacious flask (*caution!* hydrogen evolved). Nitromesitylenic acid, a by-product in the reaction, is thus reduced and brought into solution. On cooling, the undissolved portion is filtered off, washed with cold water, dissolved in dilute caustic soda, and reprecipitated from the hot filtered solution with dilute hydrochloric acid. The precipitate is a mixture of mesitylenic and uvitic acids. It is filtered off, washed with cold water and distilled in steam, till after several hours no further trace of mesitylenic acid appears in the condenser, and the distillate ceases to have an acid reaction. The greater portion of the mesitylenic acid, free from uvitic acid, is suspended in the distillate. It is filtered off and the filtrate neutralised with caustic soda solution, evaporated to small bulk, acidified with dilute hydrochloric acid, and the usually somewhat yellow-coloured acid thus obtained united to the first portion. The whole is redissolved in caustic soda solution, filtered boiling hot,

precipitated by addition of dilute hydrochloric acid, washed with cold water, and recrystallised from alcohol. It is then pure mesitylenic acid. Uvitic acid containing slight traces of mesitylenic acid separates from the residual liquid in the distilling flask on cooling. It is recrystallised from hot alcohol, after precipitation by acid from alkaline solution.

$$C_6H_3(CH_3)_3 + 3O = C_6H_3(CH_3)_2COOH + H_2O.$$
$$C_6H_3(CH_3)_2.COOH + 3O = C_6H_3(CH_3)(COOH)_2 + H_2O.$$

*Yield.—Mesitylenic acid* 50% theoretical (12 gms.). *Uvitic acid* 40% theoretical (12 gms.). *Mesitylenic acid* forms colourless monoclinic crystals; difficultly soluble in hot water; easily soluble in cold alcohol; M.P. 166°. *Uvitic acid* forms colourless fine needles; insoluble in cold and hot water; readily soluble in alcohol and ether; M.P. 287°—288°. (A., 122, 184; 141, 144; 147, 292; Z. Ch., 4, 119.)

The above illustrates the action of nitric acid in oxidising only one or two, and not all of the alkyl groups present, unless the heating is very prolonged. In the next preparation *Method I.* shows how chromic acid or alkali bichromate and sulphuric acid completely oxidises all the side chains present; *Method II.* indicates how to oxidise completely the partially oxidised compound, potassium permanganate being sufficient.

PREPARATION 186.—**Terephthalic Acid** (1 : 4-*Benzenedicarboxylic acid*).

$$C_6H_4(COOH)_2[1:4]. \qquad C_8H_6O_4. \qquad 166.$$

*Method I.* (from *p*-xylene).—20 gms. (1 mol.) of *p*-xylene are refluxed for 24 hours with 80 gms. (excess) of sodium or potassium bichromate and 250 gms. of 50% sulphuric acid. The unoxidised hydrocarbon is removed by distillation in steam, and the cooled solution filtered. The precipitate is purified by reprecipitation with acid from its dilute solution in sodium carbonate or caustic alkali.

$$C_6H_4(CH_3)_2[1:4] \xrightarrow{O_3} C_6H_4(COOH)_2[1:4].$$

*Yield.*—90% theoretical (28 gms.). (A., 133, 41.)

*Method II.* (from *p*-toluic acid).—10 gms. (1 mol.) of *p*-toluic acid (see p. 240) dissolved in 600 c.cs. (excess) of 1% caustic soda solution are refluxed on a water bath, and 5% aqueous potassium permanganate solution added until the red colour of the permanganate solution persists on boiling; for this about 500 c.cs. of potassium permanganate solution will be required. Excess of permanganate is destroyed either by adding alcohol until the liquid is colourless, the alcohol being oxidised to acetaldehyde or acetic acid, or sulphur dioxide is bubbled through the warm solution until all the manganese dioxide precipitated during the reaction dissolves. In the former method terephthalic acid is then precipitated after filtering off the manganese dioxide by addition of conc. hydrochloric acid at the boiling point, in the latter terephthalic acid is precipitated by the sulphur dioxide during the removal of excess permanganate. In both, the acid is filtered from the cooled reaction mixture, well washed

with cold water, and dried on a water bath. It is purified by reprecipitation with acid from an alkaline solution.

$$CH_3.C_6H_4.COONa + NaOH + 2KMnO_4 \\ = C_6H_4(COONa)_2 + 2KOH + MnO_2 + 2H_2O.$$

*Yield.*—90% theoretical (12 gms.). Colourless crystals; insoluble in water and in alcohol; sublimes without melting at 300°. (A., 137, 308.)

The next preparation proves how, even when two side chains form part of a ring, the oxidation follows the same course, and an *ortho*-dicarboxylic acid is obtained.

PREPARATION 187.—**Phthalic Acid** (1 : 2-*Dicarboxybenzene*).

$C_6H_4(COOH)_2$[1 : 2]. $C_8H_6O_4$. 166.

(This preparation must be carried out in a good fume cupboard.)

20 gms. (1 mol.) of naphthalene, 15 gms. of mercuric sulphate, and 350 gms. (excess) of conc. sulphuric acid are heated in a retort with its neck sealed to an air condenser acting as a reflux until all the naphthalene is dissolved. The retort is then lowered so that the air condenser slopes downwards and delivers into a receiver, cooled in water and containing 200 c.cs. of cold water. The contents of the retort are heated cautiously at first, and then vigorously at 300° until the residue in the retort is nearly dry. Unchanged naphthalene, phthalic acid and anhydride, carbon dioxide, sulphur dioxide, and water all distil. The distillate is filtered, the precipitate well washed with cold water, dissolved in caustic soda, filtered from unchanged naphthalene, reprecipitated by acidification with hydrochloric acid, and crystallised from water, or aqueous alcohol.

$$C_{10}H_8 + 9H_2SO_4 = C_6H_4(COOH)_2 + 2CO_2 + 9SO_2 + 10H_2O.$$

*Yield.*—60% theoretical (16 gms.). Colourless plates slightly soluble in cold water; soluble in alcohol and hot water; M.P. 195°; sublimes on heating to give phthalic anhydride (M.P. 128°). (D.R.P., 91202.)

The manufacture of phthalic anhydride (E.P., 249,973) from naphthalene, and maleic anhydride (U.S.P., 1,515,299) from benzene, is carried out by oxidation with air or oxygen in presence of $V_2O_5$ as catalyst.

PREPARATION 188.—***p*-Hydroxybenzoic Acid** (1-*Hydroxy*-4-*carboxybenzene*).

$C_6H_4(OH)(COOH)$[1 : 4]. $C_7H_6O_3$. 138.

10 gms. (1 mol.) of *p*-cresol are dissolved in the minimum quantity of water, and the solution heated at 70° for 10 hours with 15 gms. (excess) of potassium pyrosulphate. The crude potassium *p*-cresyl sulphate formed is heated on a water bath with 25 gms. (excess) of potassium hydroxide dissolved in 20 c.cs. of water, and 30 gms. (excess) of potassium permanganate in 750 c.cs. water gradually added. The whole is heated for 6 hours. Sulphur dioxide is then passed through the mixture to remove excess of permanganate, and the whole filtered hot. The filtrate is then boiled and acidified with hydrochloric acid, and heated to

hydrolyse the sulphuric ester. On cooling, the acid crystallises out, the remainder being obtained by extracting with ether. It is recrystallised from ether.

$$C_6H_4OH.CH_3 + 2KMnO_4 \longrightarrow C_6H_4(OH)COOH + 2MnO_2 + 2KOH.$$

*Yield.*—90% theoretical (12 gms.). Colourless crystals; soluble in hot water and in ether; M.P. 210°. (B., 19, 705.) See also O. S., XIV., 48.

PREPARATION 189.—**Anthranilic Acid** (1-*Amino-2-carboxybenzene*).

$$C_6H_4(NH_2)(COOH)[1:2]. \qquad C_7H_7O_2N. \qquad 137.$$

20 gms. (1 mol.) of aceto-*o*-toluidide (*cf.* Preparation 274) and 50 gms. (excess) of magnesium sulphate crystals are dissolved in 2½ litres of water, the mixture heated to 80°, and 60 gms. (excess) of solid, finely powdered, potassium permanganate are added with mechanical stirring; this is continued for 2 hours, during which the temperature is maintained at 85°. Excess of permanganate is removed by the addition of alcohol, the hot solution filtered, and the filtrate acidified with dilute sulphuric acid. The acetanthranilic acid precipitated is purified by reprecipitation from alkaline solution (M.P. 185°). It is hydrolysed to anthranilic acid by boiling with excess of dilute hydrochloric acid; dilute alkali can also be employed. The acid is recrystallised from hot water.

$$C_6H_4(NH.CO.CH_3)(CH_3)[1:2] + 2KMnO_4 = C_6H_4(NHCOCH_3)(COOH)[1:2] + 2MnO_2 + 2KOH.$$

$$2KOH + MgSO_4 = Mg(OH)_2 + K_2SO_4.$$

$$C_6H_4(NHCOCH_3)(COOH)[1:2] \xrightarrow{H_2O} C_6H_4(NH_2)(COOH)[1:2].$$

*Yield.*—80% theoretical (12 gms.). Colourless crystals; soluble in water and alcohol; sublimes on heating; M.P. 145°. (D.R.P., 94629.)

**Reaction CI.** (*a*) **Oxidation of Primary Alcohols to the corresponding Carboxylic Acids.** (A., 106, 79, 95; 120, 226; B., 9, 1902.)—The primary alcohols are readily oxidised through the corresponding aldehydes to carboxylic acids containing the same number of carbon atoms.

$$R.CH_2OH \longrightarrow R.CHO \longrightarrow R.COOH.$$

Chromic acid or alkali dichromate and sulphuric acid is employed for the simpler alcohols; polyhydric alcohols are usually oxidised with moderately dilute nitric acid; if the acid be too concentrated the molecule may be attacked as a whole (*cf.* Preparation 184).

PREPARATION 190.—**Acetic Acid** [*Ethan-acid*].

$$CH_3COOH. \qquad C_2H_4O_2. \qquad 60.$$

To 80 gms. (excess) of finely powdered potassium or sodium dichromate, and 100 gms. of 50% sulphuric acid placed in a reflux apparatus (see p. 212), 70 gms. (1 mol.) of 25% alcohol are slowly added. The mixture is heated for 30 minutes and distilled until only very little acid passes over. The distillate is neutralised with caustic potash, and evaporated to dryness on a water bath. The residue is powdered and distilled with conc.

sulphuric acid to 139°, and the distillate fractionated between 115° and 120°.

$$3C_2H_5OH + 2K_2Cr_2O_7 + 8H_2SO_4 = 3CH_3COOH + 2K_2SO_4 + 2Cr_2(SO_4)_3 + 11H_2O.$$

*Yield.*—80% theoretical (18 gms.). Colourless liquid or crystals; pungent odour; miscible with water; M.P. 16·7°; B.P. 119°; D. $^{15}_{4}$ 1·055.

PREPARATION 191.—**Glyceric Acid** [2 : 3-*Diol-propan-acid*].

$OH.CH_2.CH(OH).COOH.$ $C_3H_6O_4$. 106.

50 gms. (1 mol.) of glycerol diluted with an equal volume of water are treated in a tall narrow glass cylinder with 50 gms. (excess) of 90% nitric acid, the latter being carefully run in below the surface of the glycerol from a funnel, the neck of which is drawn out into a fine tube, so that two layers are formed. The whole is allowed to stand at the ordinary temperature, till after some little time the liquid becomes homogeneous. The contents of several (six) such cylinders are slowly evaporated on a water bath to a syrup, 2 litres of water are added, and the solution (*a*) neutralised with lead carbonate and a small quantity of lead oxide. Towards the end of the operation the liquid is boiled and filtered hot. Crude lead glycerate separates on concentrating and cooling the filtrate. The salt which adheres firmly to the side of the vessel is detached by warming. A second crop of crystals slowly separates on concentrating the mother liquors. The finely powdered salt made into a paste with water is treated with hydrogen sulphide in 2·5 gm. lots, and the solution, filtered from lead sulphide, evaporated on a water bath, when the acid remains as a thick syrup.

The aqueous solution (*a*) may also be worked up for glyceric acid by boiling it with excess of calcium carbonate and filtering hot. The calcium glycerate, which separates on cooling and concentrating, is recrystallised from hot water, suspended in water, and decomposed by treatment with the theoretical quantity of oxalic acid (determined on estimating the calcium by ignition in a sample of the salt). The clear solution filtered from calcium oxalate is evaporated as above.

$$(OH)CH_2.CH(OH)CH_2(OH) + O_2 = (OH)CH_2CH(OH)COOH + H_2O.$$

*Yield.*—80% theoretical (275 gms. from 300 gms. of glycerol). Strongly acid syrup, faintly yellow colour; soluble in water, alcohol and acetone; insoluble in ether; decomposes on boiling. (A., 106, 79, 95; 120, 226; B., 9, 1902.)

**Reaction CI.** (*b*) **Oxidation of Aldehydes to Carboxylic Acids.** (B., 17, 1298; 24, 521; A., 227, 224.)—The aldehydes are very readily oxidised to the corresponding acids; in the oxidation of primary alcohols to acids, it is the first stage which is the more difficult to achieve. A great variety of oxidising agents may be employed—nitric acid is used for the less complex aldehydes, *e.g.*, chloral to trichloroacetic acid; in the sugar group bromine gives very good results (see below).

$$R.CHO + O = R.COOH.$$

PREPARATION 192.—**Gluconic Acid** (*Pentol-hexan acid* + − + +).

$$\begin{array}{l} \quad COOH \\ \;H.\dot{C}.OH \\ HO.C.H \\ \;H.\dot{C}.OH \\ \;H.\dot{C}.OH \\ \quad \dot{C}H_2OH. \end{array} \qquad C_6H_{12}O_7. \qquad 196.$$

50 gms. (1 mol.) of glucose dissolved in 400 c.cs. of water are treated in a stoppered bottle with 100 gms. (excess) of bromine. The mixture is allowed to stand, with frequent shaking, for 3 days at ordinary temperatures, and then boiled in a porcelain dish in a fume cupboard with constant stirring, until all the bromine has disappeared. The solution is cooled, diluted with water to 500 c.cs., and neutralised with lead carbonate suspended in water. The precipitate is filtered at the pump, suspended in water and saturated with hydrogen sulphide, filtered and neutralised by boiling for ½ hour with precipitated chalk. The filtrate is evaporated to about 100 c.cs., and seeded in the cold with a crystal of calcium gluconate. After 24 hours the whole is filtered at the pump and the precipitate washed with cold water, redissolved in a small quantity of hot water, and boiled with addition of animal charcoal. The latter is filtered off and the solution treated with the exact quantity of oxalic acid in aqueous solution necessary to precipitate the calcium present, a portion of the precipitate obtained above being ignited and the calcium in it estimated for the purpose. The precipitated calcium oxalate is filtered off and washed, and the washings and filtrate evaporated to a syrup on a warm water bath under reduced pressure.

$$C_5H_{11}O_5CHO + H_2O + Br_2 = C_5H_{11}O_5COOH + 2HBr.$$

*Yield.*—50% theoretical (30 gms.). Acid syrup; soluble in water; on standing or heating changes in part to a crystalline lactone; M.P. 130°—135°. (B. 17, 1298.)

This preparation is important in the sugar group, as it is possible to pass from one stereoisomeric acid to another by heating with pyridine—this enables the corresponding sugars to be transformed one into another by oxidation to the acid, transformation of the acid to its stereoisomer, and reduction of the lactone of the latter acid (see p. 190).

PREPARATION 193.—**Saccharic Acid** (*Tetrol-hexan-diacid* + − + +).

$$COOH.(CHOH)_4.COOH. \qquad C_6H_{10}O_8. \qquad 210.$$

50 gms. (1 mol.) of anhydrous glucose are heated in a dish on a water bath with 350 gms. (excess) of 25% nitric acid and, while stirred mechanically, are evaporated to a syrup, which is dissolved in a little water, and again evaporated. Should the mass begin to show the slightest sign of charring, heating is immediately discontinued. The whole is dissolved in 200 c.cs. of water, and neutralised with a saturated solution of potassium carbonate. 25 c.cs. of 50% acetic acid are added and the liquid evaporated to about 75 c.cs. On frequent rubbing and long standing in the

cold, acid potassium saccharate crystallises out, and is filtered at the pump after a further 12 hours' standing, washed with a very little cold water, and recrystallised from hot water with addition of animal charcoal; if not quite colourless, the operation is repeated. The salt is treated with excess of 10% hydrochloric acid and evaporated on a warm water bath under reduced pressure to a deliquescent mass, which is treated with absolute alcohol, filtered, and the filtrate evaporated under reduced pressure till all the alcohol is removed.

$$\begin{array}{c}CH_2OH\\ |\\ (CHOH)_4\\ |\\ CHO\end{array} \longrightarrow \begin{array}{c}COOH\\ |\\ (CHOH)_4\\ |\\ COOH.\end{array}$$

*Yield.*—20% theoretical (12 gms.). Colourless deliquescent mass; soluble in water; very soluble in alcohol; changes on standing to a crystalline lactone (M.P. 131°). (B., 24, 521.)

This preparation illustrates the oxidation of a carboxylic acid, both of a primary alcohol and an aldehyde. The reaction also is of importance in the sugar group, for it is possible to reduce the carboxyl group in saccharic acid which comes from the aldehyde group to a primary alcohol group, while the carboxyl corresponding to the primary alcohol group is reduced to an aldehyde. In this way a new sugar stereoisomeric with the first may be obtained.

Following is one of the applications of the method—

$$\begin{array}{lllll}
\underset{\text{Glucose}}{(+-++)} & \longrightarrow & \underset{\text{Gluconic acid}}{(+-++)} & \longrightarrow & \underset{\text{Saccharic acid}}{(+-++) \text{ or } (++-+)} \longrightarrow \\
\underset{\text{Gulonic acid}}{(++-+)} & \longrightarrow & \underset{\text{Gulose.}}{(++-+)} & &
\end{array}$$

The next preparation illustrates the hydrolysis of a disaccharose, and the simultaneous oxidation of the monosaccharoses so formed.

PREPARATION 194.—**Mucic Acid** (*Tetrol-hexan-diacid* + − − +).

$$\begin{array}{c}COOH\\ H.\dot{C}.OH\\ OH.\dot{C}.H\\ OH.\dot{C}.H\\ H.\dot{C}.OH\\ \dot{C}OOH\end{array} \qquad C_6H_{10}O_8. \qquad 210.$$

100 gms. (1 mol.) of lactose are heated on a water bath with 1,500 gms. (excess) of 25% nitric acid, the whole being continuously stirred, until the volume is reduced to 250 c.cs. The cooled acid mass is diluted with 750 c.cs. of water, filtered at the pump, well washed with cold water, and dissolved in just sufficient N/1 caustic soda solution (excess tends to reprecipitate the sodium salt). The latter solution is warmed with animal charcoal and filtered, and the acid reprecipitated by addition of the

equivalent in 5N hydrochloric acid of the N/1 caustic soda used for solution. During this addition the temperature must not rise above 15°, otherwise the lactone of the acid may be formed. The whole is kept for 12 hours in a freezing mixture, and the precipitate filtered at the pump, well washed with cold water and dried on a water bath.

$$\underset{\text{Lactose.}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Glucose.}}{C_6H_{12}O_6} + \underset{\text{Galactose.}}{C_6H_{12}O_6}.$$

$$\underset{\text{Glucose.}}{C_6H_{12}O_6} \xrightarrow{O_2} \underset{\text{Saccharic acid.}}{C_6H_{10}O_8}.$$

$$\underset{\text{Galactose.}}{C_6H_{12}O_6} \xrightarrow{O_2} \underset{\text{Mucic acid.}}{C_6H_{10}O_8}.$$

Saccharic acid being soluble in water remains in solution.

*Yield.*—55% theoretical (32 gms.). White crystalline powder; almost insoluble in cold water and in alcohol; M.P. 210° (with decomposition). (A., 227, 224.)

# CHAPTER XVII

## OXYGEN TO CARBON

## Oxide-Oxy Compounds

### Esters and Acid Anhydrides

This section deals first with the preparation of alkyl acyl oxide compounds—esters—by the interaction of an acid or an acid derivative and an alcohol. The fact that the formation of an ester and water from a mixture of an acid and an alcohol is a reversible reaction necessitates special measures being adopted to displace the equilibrium towards the more complete formation of ester.

The second portion of the section discusses the preparation of di-acyl oxide compounds—acid anhydrides.

**Reaction CII. Direct Action of an Acid on an Alcohol.** (A. Ch., 58, 44.) —Few normal esters are prepared in this way—dimethyl oxalate being an exception; in this case the water formed is probably prevented from including the back reaction by the presence of anhydrous oxalic acid—but the yield is only 40%. With acid esters, however, good yields can be obtained, since only partial esterification is required.

$$R.\left\langle\begin{matrix}COOH\\COOH\end{matrix}\right. + R_1OH = R\left\langle\begin{matrix}COOR_1\\COOH\end{matrix}\right. + H_2O.$$

Preparation 195.—**Dimethyl Oxalate** [*Dimethyl ester of ethan-diacid*].

$$\begin{matrix}COO.CH_3\\|\\COO.CH_3\end{matrix} \qquad C_4H_6O_4. \qquad 118.$$

In order to prevent hydrolysis of the ester as it is formed, it is necessary in this preparation to use *anhydrous* oxalic acid and to purify and dry the methyl alcohol as described on p. 213.

63 gms. (1 mol.) of oxalic acid crystals are powdered and heated on a boiling water bath till no more water is given off (1—2 hours), and are then heated in an air oven at 110°—120° until the required loss in weight (18 gms.) has taken place. During the heating, the acid should be powdered occasionally. The *anhydrous acid* is refluxed on a water bath with 50 gms. (excess) of *pure anhydrous* methyl alcohol for $2\frac{1}{2}$ hours, excess alcohol removed on a water bath, and the residue distilled to 120°; the water is run out of the condenser, and the fraction 160°—165° col-

lected. The solid portion is filtered off, dried on a porous plate, and recrystallised from methyl or ethyl alcohol.

$$\begin{array}{l}COOH\\|\\COOH\end{array} + 2CH_3.OH = \begin{array}{l}COOCH_3\\|\\COOCH_3\end{array} + 2H_2O.$$

*Yield.*—40% theoretical (25 gms.). Colourless plates; somewhat soluble in alcohol; M.P. 54°; B.P. 163°. (A. Ch., 58, 44; O. S., X., 78.)

In the next preparation the forward reaction is assisted by removal of the ester as fast as it is produced (*cf.* Reaction CIII.). This is only possible when a strong acid is present to act as a catalyst—the hydrogen ions cause fresh ester to be formed rapidly. It is necessary that the ester should be volatile, or in some other manner readily removable from the sphere of the reaction.

PREPARATION 196.—**Ethyl Nitrate** (*Ethyl-ester of nitric acid*).

$$CH_3.CH_2.O.NO_2. \qquad C_2H_5O_3N. \qquad 91.$$

To 20 gms. (1 mol.) of cold "boiled-out" 67% nitric acid, 2 gms. of urea in 15 gms. (excess) of absolute alcohol are added, and half of the mixture distilled off on a water bath in a tubulated retort attached to condenser and receiver. 40 gms. of similar nitric acid mixed with 30 gms. of absolute alcohol, and containing 0·5 gm. of urea, are now allowed to drop in through the tubulus from a tap funnel at the same rate as the liquid distils. Water is added to the distillate, the ester which separates is washed several times with cold water, dried over calcium chloride, and distilled from a water bath, the fraction 84°—88° being retained. Care must be taken in this experiment, as the ester is liable to explode when quickly heated. All operations should be carried out behind a metal screen.

$$C_2H_5OH + HNO_3 = C_2H_5NO_3 + H_2O.$$

*Yield.*—75% theoretical (22 gms.). Colourless liquid; characteristic odour; *liable to explode when quickly heated;* B.P. 86°; D. $^{15}_{4}$ 1·112.

Urea is used above to decompose any nitrous acid formed, as the presence of the latter tends to cause explosion.

$$CO(NH_2)_2 + 2HNO_2 = CO_2 + 2N_2 + 3H_2O.$$

(B., 14, 421.)

The following illustrates the preparation of acid esters.

PREPARATION 197.—**Ethyl Hydrogen Tartrate** [*Monoethyl ester of* 2 : 3-*butandiol-diacid*].

$$\begin{array}{l}CH(OH).COOH\\|\\CH(OH).COOC_2H_5\end{array} \qquad C_6H_{10}O_6. \qquad 178.$$

20 gms. (1 mol.) of finely powdered tartaric acid and 30 gms. (excess) of *absolute* alcohol are heated for 6 hours at 70° on a water bath in a reflux apparatus. An equal volume of water and then an excess of powdered barium carbonate are added, and the liquid filtered from barium tartrate and excess of barium carbonate. The filtrate is evaporated to crystal-

lisation on a water bath, cooled, and the crystals of barium ethyl-tartrate which separate filtered off at the pump and dried on a porous plate. They are weighed and treated with the theoretical amount of 2N sulphuric acid to precipitate the barium present, barium sulphate is filtered off, and the filtrate evaporated to crystallisation point. The crystals which separate are recrystallised from a little water.

$$\begin{array}{l}CH(OH)COOH\\ |\\ CH(OH)COOH\end{array} + C_2H_5.OH = \begin{array}{l}CH(OH)COOC_2H_5\\ |\\ CH(OH)COOH\end{array} + H_2O.$$

*Yield.*—70% theoretical (17 gms.). Colourless crystals; somewhat soluble in water; M.P. 90°. (A., 22, 248.)

By a repetition of the above process, using the alkyl hydrogen tartrate, diethyl tartrate can be obtained, but the yield is poor.

When conc. sulphuric acid acts on the alcohols, the acid esters only are formed, though sulphuric acid, by its great affinity for water, promotes almost complete esterification in other instances; for the preparation of normal sulphuric esters, see Preparation 210.

**Reaction CIII. Esterification with Continuous removal of Water.** (P. R. S., 25, 831; J. C. S., 87, 1657.)—In this method, which requires little elaboration, it is necessary that the acid and ester have high boiling points compared with that of water. The last is continually volatilised with the alcohol and circulated over a dehydrating agent which absorbs it—the alcohol being returned to the reaction vessel.

PREPARATION 198.—**Diethyl Tartrate** [*Diethyl ester of* 2 : 3-*butandiol-diacid*].

$$\begin{array}{l}CH(OH)COOC_2H_5\\ |\\ CH(OH)COOC_2H_5.\end{array} \qquad C_8H_{14}O_6. \qquad 206.$$

*Method I.*—The apparatus described in Preparation 1 is fitted up, a 500-c.c. flask being used, and 30 gms. (1 mol.) of finely powdered tartaric acid, 150 gms. (excess) of absolute alcohol, and 50 gms. of crystallised benzene placed in the flask. The object of the benzene is to help to volatilise the water produced by forming with it and the alcohol the low boiling ternary system—alcohol-benzene-water. The iron tube is packed with small lumps of good quicklime, and is heated to a temperature of 90°. The mixture in the flask is boiled, a few pieces of porous porcelain being added to promote steady ebullition. Esterification proceeds almost to completion, owing to the removal by the quicklime of the water formed. After 6 hours, the liquid in the flask, which will have become quite viscid owing to the formation of the ester, is distilled on a water bath until all the benzene and excess of alcohol have been removed; the residue is fractionated from a metal bath under reduced pressure.

*Yield.*—90% theoretical (37 gms.). (P. R. S., 25, 831; J. C. S., 87, 1657.)

*Method II.*—The apparatus (Fig. 48) is fitted up, being held in position by a clamp holding the condenser C. In the flask A are placed 150 gms. of tartaric acid (or other acid to be esterified), which need not be specially

dried or powdered, and which is just covered with alcohol. B contains 140 gms. (3 mols.) of the latter, and 100 gms. of fresh potassium carbonate or other suitable solid desiccating agent. The apparatus communicates with the open air only by means of the tube E. A is immersed to the neck in an oil bath which is slowly heated to 130°, and as soon as most of the alcohol in it has distilled into B, the latter is heated on a boiling water bath. The alcohol in B passes up the fractionating column D, which assists the action of the dehydrating agent, and into A, from which uncombined alcohol, and the water formed in the esterification, distil into B. After 10 hours, the excess of alcohol is distilled off from A, and the residue fractionated from a metal bath under reduced pressure.

$$(CH(OH)COOH)_2 + 2C_2H_5OH = (CH(OH)COOC_2H_5)_2 + 2H_2O.$$

*Yield.*—80% theoretical (165 gms.). (J. C. S., 79, 517.)

Colourless crystals ; insoluble in water ; miscible with alcohol. M.P. 18·7° ; B.P. $^{11}$ 155° ; B.P. $^{23}$ 164° ; D. $^{0}_{4}$ 1·072.

For other methods of preparation and method of purification, see J. C. S., 121, 532.

**Reaction CIV. Use of Concentrated Sulphuric Acid or of Hydrogen Chloride to promote Esterification.** (B., 13, 1176 ; 28, 1150, 3252 ; Phil. Trans., 156, 37 ; Bl., 33, 350 ; J., (1874), 352 ; A., 204, 126.)—Conc. sulphuric acid being a dehydrating agent is frequently used to promote esterification ; it also acts as a catalyst increasing the speed of the reaction. Saturation of the alcohol with hydrogen chloride has also been employed with the same end in view, but it has been found that 4% hydrogen chloride in the alcohol gives even better results. Hence it is probable that this acid acts catalytically and not as a dehydrating agent.

PREPARATION 199.—**Ethyl Acetate** [*Ethyl ester of ethan acid*].

$$CH_3.COOC_2H_5. \qquad C_4H_8O_2. \qquad 88.$$

200 c.cs. of a mixture of equal volumes of glacial acetic acid (1 mol.), and absolute alcohol (1 mol.) are added, drop by drop at the same speed as the liquid distils, to a mixture of 50 c.cs. of conc. sulphuric acid and 50 c.cs. (excess) of absolute alcohol in a distilling flask attached to a condenser and receiver and heated in an oil bath kept at 140°. The distillate is shaken in an *open* tap funnel with aqueous sodium carbonate solution until the upper layer is no longer acid to moistened blue litmus paper. This layer is shaken with 50 c.cs. of a 50% aqueous solution of calcium chloride to remove alcohol, and then allowed to stand 24 hours in contact with calcium chloride. It is filtered through a dry filter paper and fractionated on a water bath, the fraction 73°—80° being redistilled.

$$CH_3COOH + C_2H_5OH = CH_3COOC_2H_5 + H_2O.$$

*Yield.*—85% theoretical (130 gms.). Colourless liquid ; characteristic odour ; somewhat soluble in water ; miscible with alcohol, ether and acetic acid ; B.P. 78° ; D. $^{15}_{4}$ 0·9068 ; Phil. Trans., 156, 37 ; Bl., 33, 350 ; J. S. C. I., 43, 295.

Methyl acetate (B.P. 57°, D. $^{20}_{4}$ 0·904) is prepared in a similar manner from methyl alcohol.

PREPARATION 200.—**Diethyl Tartrate** [*Diethyl ester of* 2 : 3-*butandiol-diacid*].

$$(CH(OH)COOC_2H_5)_2. \qquad C_8H_{14}O_6. \qquad 206.$$

50 gms. (1 mol.) of finely powdered tartaric acid are refluxed on a water bath with 150 c.cs. (excess) of absolute alcohol until dissolved, and the solution saturated with hydrogen chloride at 0°. After 12 hours it is heated under reduced pressure on a water bath to remove hydrogen chloride, excess of alcohol and water, and the residue, which consists chiefly of ethyl hydrogen tartrate, treated with a further 150 c.cs. (excess) of absolute alcohol, the mixture again saturated with hydrogen chloride at 0°, and allowed to stand for 12 hours. It is then fractionated under reduced pressure, and the fraction, B.P. $^{11}$ 152°—158° or B.P. $^{18-20}$ 159°—168°, refractionated under reduced pressure.

*Yield.*—80% theoretical (55 gms.). Colourless crystals; M.P. 18·7°; insoluble in water; miscible with alcohol; B.P. $^{11}$ 155°; B.P. $^{23}$ 164°; D. $^{0}_{4}$ 1·072. (B., 13, 1176; J. C. S., 79, 168.)

The above exemplifies the old method of saturation of the mixture with hydrogen chloride; the Fischer-Speir modification, illustrated in the following preparation, can be employed; the time for the preparation is shortened, and only half the above quantity of alcohol is required.

PREPARATION 201.—**Ethyl Benzoate** (*Ethyl ester of benzoic acid*).

$$C_6H_5.COOC_2H_5. \qquad C_9H_{10}O_2. \qquad 150.$$

150 gms. (excess) of absolute alcohol are cooled in ice, and dry hydrogen chloride bubbled through it until an increase in weight of 6 gms. has been obtained. 50 gms. (1 mol.) of benzoic acid are added, and the whole refluxed for 2 hours until on pouring a sample into water no benzoic acid separates. The excess of alcohol is removed on a water bath, the residue diluted with 2 volumes of water, and the whole shaken in an open vessel with solid sodium carbonate until any acid present is removed. The ester is then extracted with ether, the extract dried for 24 hours over *pure* potassium carbonate and fractionated, the fraction 204°—213° being redistilled. The carbonate should be made by heating the bicarbonate, in order to ensure its being pure and anhydrous.

$$C_6H_5.COOH + C_2H_5OH = C_6H_5COOC_2H_5 + H_2O.$$

*Yield.*—80% theoretical (49 gms.). Colourless oil; sweetish odour; insoluble in water; miscible with alcohol and ether; B.P. $^{760}$ 211°; D. $^{15}_{4}$ 1·05. (B., 28, 1150.)

The above compound can also be made using 10 gms. of conc. sulphuric acid, 100 gms. of absolute alcohol, and 50 gms. of benzoic acid. Although less alcohol is used, the yield is 90% theoretical, being increased by the dehydrating action of the sulphuric acid. Methyl benzoate (B.P. 199°) can be prepared in a similar manner.

The following exemplifies the preparation of an ester by the above methods, using a salt of an acid from which the mineral acid present

liberates the free acid. This modification is especially useful when the acid to be esterified is difficult to isolate in a free state.

PREPARATION 202.—**Diethyl Malonate** [*Diethyl ester of propan-diacid*].

$$CH_2(COOC_2H_5)_2. \qquad C_7H_{12}O_4. \qquad 160.$$

For this esterification 250 c.cs. (excess) of absolute alcohol are employed to 100 gms. of hydrated calcium malonate, which has been dried as completely as possible on a water bath, or to 95 gms. of the anhydrous salt of the acid. It is better to use the latter. 20 gms. of the dried salt are placed in a litre flask, all the absolute alcohol is poured on to it, and a stream of well-dried hydrogen chloride is passed in, so that the liquid becomes warm. The remainder of the calcium salt is added in 15-gm. lots as fast as the previous portion disappears. By this means caking of the calcium salt is prevented. The complete solution should take about 30 minutes, by which time the alcoholic liquid will be saturated with hydrogen chloride. After standing for 24 hours, the solution is evaporated to a small volume under reduced pressure, and the residual ester dissolved in ether. The ethereal solution is dried over calcium chloride, the ether removed on a water bath, and the residue fractionated, the fraction 195°—198° being retained.

$$CH_2(COO)_2Ca + 2HCl + 2C_2H_5OH = CH_2(COOC_2H_5)_2 + CaCl_2 + 2H_2O.$$

*Yield.*—75% theoretical (65 gms.). Colourless liquid; B.P. (uncorr.) 195°; B.P. (corr.) 197°—198°; D. $^{18}_{4}$ 1·068. (A., 204, 126.)

PREPARATION 203.—**Amyl Nitrite** (*Amyl ester of nitrous acid*).

$$O:N.O.C_5H_{11}. \qquad C_5H_{11}O_2N. \qquad 117.$$

30 gms. (2 mols.) of amyl alcohol and 25 gms. (excess) of sodium nitrite are treated in a 500-c.c. round-bottomed flask cooled in ice, with 30 gms. (excess) of conc. sulphuric acid added drop by drop with constant shaking. The addition must be carried out in a fume cupboard, and care must be taken not to inhale the vapour of the amyl nitrite. When all the acid is added, the top layer of ester is separated and the residue shaken with water; the further quantity of ester which separates is added to that first obtained, and the whole washed with water, separated, dried for 24 hours over calcium chloride and distilled, the fraction 94°—101° being redistilled.

$$2C_5H_{11}OH + 2NaNO_2 + H_2SO_4 = 2C_5H_{11}ONO + Na_2SO_4 + 2H_2O.$$

*Yield.*—75% theoretical (30 gms.). Greenish-yellow liquid; characteristic odour; insoluble in water; miscible with ether and alcohol; B.P. $^{760}$ 96°; D. $^{0}_{4}$ 0·902. (J., (1874), 352.) See also O. S., XVI., 8.

**Reaction CV. Action of Acid Anhydrides on Alcohols and Phenols.** (B., 12, 2059; 21, 1172; J. C. S., 1931, 2495.)—The method is employed when the acids themselves do not react and is useful for the rapid preparation of acetates of alcohols and phenols and for the acetylation of cellulose.

$$2R_1OH + (R_{11}CO)_2O = 2R_{11}COOR_1 + H_2O.$$

Esterification is effected in the cold in presence of alkali or by heating the alcohol and anhydride together, usually in presence of a dehydrating agent—*e.g.*, fused zinc chloride, anhydrous sodium acétate, etc.

PREPARATION 204.—**Mannitol Hexacetate.**

$$(CH_2O.COCH_3)(CHO.COCH_3)_4(CH_2O.COCH_3). \qquad C_{18}H_{26}O_{12}. \qquad 434.$$

10 gms. of mannitol, 10 gms. of fused sodium acetate, and 40 gms. acetic anhydride are placed in a small flask provided with a reflux condenser and heated, at some distance above a wire gauze, to gentle boiling for an hour. The product is poured into water, well stirred and broken up with a glass rod. After some time it is filtered off, washed with water, and recrystallised from alcohol.

$$CH_2OH(CHOH)_4CH_2OH + 3(CH_3CO)_2O \longrightarrow C_{18}H_{26}O_{12} + 3H_2O.$$

*Yield.*—Almost theoretical (24 gms.). Colourless crystals; insoluble in water; soluble in hot alcohol; M.P. 119°. (B., 12, 2059.)

The above preparation represents a general method for the preparation of acetyl derivatives of hydroxy compounds. Fused zinc chloride may be used in place of fused sodium acetate, but charring of the product is more likely to occur.

The next preparation illustrates the action of the anhydride of a dibasic acid.

PREPARATION 205.—**Methyl Hydrogen Succinate** [*Monomethyl-ester of butan-diacid*].

$$\begin{array}{l} CH_2COOCH_3 \\ | \\ CH_2COOH. \end{array} \qquad C_5H_8O_4. \qquad 132.$$

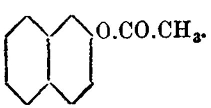
10 gms. (1 mol.) of succinic anhydride (see p. 266) are refluxed with 10 gms. (excess) of pure methyl alcohol (see p. 213) for 1 hour, excess of alcohol is removed under reduced pressure at ordinary temperature, and the residue recrystallised from hot carbon disulphide (*Caution!*).

$$\left.\begin{array}{l} CH_2CO \\ | \\ CH_2CO \end{array}\right\rangle O + CH_3OH = \begin{array}{l} CH_2CO.OCH_3 \\ | \\ CH_2CO.OH. \end{array}$$

*Yield.*—Almost theoretical (13 gms.). Glistening plates; insoluble in water; M.P. 57°; B.P.$^{20}$ 151°.

Phenols and naphthols also can be readily acetylated, using acetic anhydride. The general method is shown in the next preparation.

PREPARATION 206.—**β-Naphthyl Acetate** (2-*Acetoxynaphthalene*).



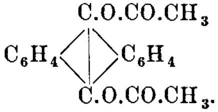

$C_{12}H_{10}O_2$. 186.

To a solution of 10 gms. of β-naphthol in 50 c.c. of 10% caustic soda solution 100 gms. of crushed ice are added, followed by 12 gms. of acetic anhydride. The product is crystallised from aqueous alcohol.

$$2C_{10}H_7OH + (CH_3CO)_2O = 2C_{10}H_7O.COCH_3 + H_2O.$$

*Yield.*—Theoretical (13·5 gms.). Colourless crystals; insoluble in water; M.P. 70°. (A., 209, 150; J. C. S., 1931, 2495.)

PREPARATION 207.—**9 : 10-Diacetoxyanthracene.**



$C_{18}H_{14}O_4$. 294.

10 gms. (1 mol.) of anthraquinone are refluxed and agitated for 30 minutes with 150 gms. (excess) of acetic anhydride, 10 gms. of fused sodium acetate (see p. 509), and 40 gms. (excess) of zinc dust, and the cooled mixture filtered at the pump. The product, which is the result of reduction and acetylation, is recrystallised three times from glacial acetic acid.

$$C_6H_4(CO)_2C_6H_4 + (CH_3CO)_2O + H_2 = (C_6H_4)(CO.COCH_3)_2C_6H_4 + H_2O.$$

*Yield.*—Almost theoretical (14 gms.). Colourless needles; insoluble in water; M.P. 260°. (B., 21, 1172.)

**Reaction CVI. Action of Acyl Chlorides on Alcohols.** (B., 17, 2545; 19, 3218; 21, 2744; 23, 2962; A., 245, 140; 301, 102; 327, 105; J. pr., [2], 20, 263.)—Acid chlorides, especially of the aliphatic series, react with alcohols and phenols to give esters.

$$R_1.OH + R_{11}CO.Cl = R_{11}.CO.OR_1 + HCl.$$

With aromatic acyl chlorides the reaction is not so rapid, but it can be greatly facilitated by the presence of caustic soda or caustic potash in dilute aqueous solution (Schotten-Baumann).

$$R_1OH + R_{11}CO.Cl + NaOH = R_{11}.CO.OR_1 + NaCl + H_2O.$$

Other alkalis can be employed—carbonates of the alkali and alkaline earth metals—pyridine, too, gives very good results, though with polyhydric alcohols the number of groups esterified may differ with organic and inorganic bases. Acetyl and similar aliphatic derivatives of hydroxy compounds cannot be prepared in this way, owing to the great instability of the acyl chlorides in presence of alkali.

The Schotten-Baumann reaction can also be applied to primary and secondary aromatic amines (see p. 303); it is much used in the identification of compounds to which it can be applied, by the preparation of their benzoyl, phenylacetyl, or benzene sulphonyl derivatives.

PREPARATION 208.—**Ethyl Acetate** [*Ethyl ester of ethan acid*].

$CH_3.COO.C_2H_5$. $C_4H_8O_2$. 88.

To 10 gms. (excess) of absolute alcohol, 15 gms. (1 mol.) of acetyl chloride (see p. 332) are added drop by drop with good cooling and shaking, the temperature not being allowed to rise above 20°. The whole is carefully diluted with an equal volume of saturated brine, and the ethyl acetate which floats on the surface separated, well washed with a 50% solu-

tion of calcium chloride to remove alcohol, dried for 24 hours over calcium chloride, and fractionated, the fraction 74°—81° being redistilled.

$$CH_3COCl + C_2H_5OH = CH_3.COOC_2H_5 + HCl.$$

*Yield.*—Almost theoretical (16 gms.) (see p. 256).

PREPARATION 209.—**Ethyl-3 : 5-Dinitrobenzoate.**

$(NO_2)_2C_6H_3COOC_2H_5$. $C_9H_8O_6N_2$. 240.

5 gms. of 3 : 5-dinitrobenzoic acid and 5 gms. of phosphorus pentachloride are gently warmed and the mixture allowed to cool. The solid dinitrobenzoyl chloride is separated from the phosphorus oxychloride by pressing on a porous plate. The crude chloride is then treated with 5 c.cs. of ethyl alcohol, under reflux, and warmed to about 80° for 10 minutes. The product is crystallised from 60% alcohol. M.P. 92°. (A., 202, 223.)

The above is the procedure for the preparation of dinitrobenzoates, so useful for the identification of alcohols.

PREPARATION 210.—**Dimethyl Sulphate** (*Dimethyl ester of sulphuric acid*).

$(CH_3)_2SO_4$. $C_2H_6O_4S$. 126.

(Dimethyl sulphate is *very poisonous, and great care must be taken not to inhale its vapour. Ammonia vapour neutralises the toxic effects. This preparation must be carried out in a good fume cupboard.*)

100 gms. (excess) of chlorosulphonic acid (see p. 511) are placed in a 250-c.c. distilling flask fitted with a rubber stopper, carrying a thermometer the bulb of which is immersed in the acid, and cooled to − 10° ; 30 gms. (excess) of pure anhydrous methyl alcohol are slowly dropped in during 2 hours by means of a dropping funnel, the stem of which is drawn out to a fine point, and then bent upwards so that the opening is just below the surface of the acid in the flask. Care must be taken that initially the stem of the funnel is full of alcohol. The side tube of the flask is connected with three wash-bottles, the first containing conc. sulphuric acid, and the third cold water to absorb the hydrogen chloride evolved ; the second is empty, and reversed to prevent the water sucking back into the sulphuric acid. During the addition, the flask is frequently shaken, and throughout, the temperature must not be allowed to rise above − 10°. When all the alcohol has been added, the mixture is cautiously distilled at 20 mms. from an oil bath at 140°. The ester which comes over is washed with a little ice-water, dried over anhydrous sodium sulphate for 24 hours, and re-distilled at 20 mms. as before, collecting at 150°—160°.

$$Cl.SO_2.OH + 2CH_3.OH = SO_2(OCH_3)_2 + HCl + H_2O.$$

Methyl hydrogen sulphate, formed at an intermediate stage, yields the normal sulphate on vacuum distillation.

*Yield.*—90% theoretical (50 gms.). Colourless odourless liquid ; emits very poisonous vapour ; B.P. $^{760}$ 188°. (A., 327, 105.)

Methyl ethyl sulphate can be prepared by adding ethyl chlorosulphonate

to sodium methoxide in dry ether (Am. Soc., 46, 1044), and other alkyl sulphates can be prepared by a similar method (C. r., 178, 1182).

PREPARATION 211.—**Dimethyl Terephthalate** (*Dimethyl ester of* 1 : 4-*benzenedicarboxylic acid*).

$$C_6H_4(COOCH_3)_2[1:4]. \qquad C_{10}H_{10}O_4. \qquad 194.$$

10 gms. (1 mol.) of terephthalic acid (see p. 246) are warmed with 13 gms. (2 mols.) of phosphorus pentachloride until liquefaction occurs, 20 gms. (excess) of methyl alcohol are added, and the whole refluxed for 2 hours. On cooling, the precipitate is filtered off and recrystallised from methyl alcohol.

$$C_6H_4(COOH)_2 \xrightarrow{PCl_5} C_6H_4(COCl)_2 \xrightarrow{CH_3OH} C_6H_4(COOCH_3)_2.$$

*Yield.*—80% theoretical (9 gms.). Colourless crystals; insoluble in water; M.P. 140°. (A., 245, 140; J. pr., [2], 20, 263; D.R.P., 38973; 70483; 71446.)

Sodium terephthalate can be used alone in place of the free acid.

The following preparations exemplify the Schotten-Baumann reaction.

PREPARATION 212.—**Methyl Benzoate** (*Methyl ester of benzenemonocarboxylic acid*).

$$C_6H_5COOCH_3. \qquad C_8H_8O_2. \qquad 136.$$

20 gms. (excess) of methyl alcohol are added to 15 gms. (1 mol.) of benzoyl chloride and then 10% caustic soda solution, until the whole is alkaline. The mixture is well shaken, warmed gently, until the smell of benzoyl chloride has completely disappeared, and poured into water. The layer of ester is dissolved in ether, the solution dried over calcium chloride, and distilled, the fraction 195°—205° being redistilled.

$$C_6H_5.COCl + CH_3OH + NaOH = C_6H_5COOCH_3 + NaCl + H_2O.$$

*Yield.*—90% theoretical (12 gms.). Colourless liquid; B.P. $^{760}$ 199°; D. $^{10}_{4}$ 1·1086. (B., 17, 2545; 19, 3218; 21, 2744; 23, 2962.)

Ethyl benzoate, glyceryl tri-benzoate, etc., are prepared in an exactly similar manner. The reaction can also be applied to phenols and naphthols.

PREPARATION 213.—**Phenyl Benzoate** (*Phenyl ester of benzenemonocarboxylic acid*).

$$C_6H_5COOC_6H_5. \qquad C_{13}H_{10}O_2. \qquad 198.$$

10 gms. (excess) of phenol are dissolved in 100 c.cs. of water and 10 gms. (1 mol.) of benzoyl chloride added, and then 10% aqueous caustic soda solution until the whole is alkaline. The mixture is warmed and shaken until the smell of benzoyl chloride has disappeared; the ester which separates is filtered off at the pump, washed with cold water, dried on a porous plate, and recrystallised from alcohol.

$$C_6H_5.CO.Cl + C_6H_5OH + NaOH = C_6H_5COOC_6H_5 + NaCl + H_2O.$$

*Yield.*—Almost theoretical (21 gms.). Colourless crystals; insoluble in water; M.P. 68°. (B., 17, 2545; 19, 3218; 21, 2744; 23, 2962.)

$\alpha$- and $\beta$-naphthyl benzoates (M.P. 56° and 107° respectively) are similarly prepared. Pyridine is the base used in the next preparation.

PREPARATION 214.—**Mannitol Dibenzoate** [1 : 6-*Dibenzoic ester of hexol-hexan*].

$$C_6H_8(OH)_4(O.OC.C_6H_5)_2. \qquad C_{20}H_{22}O_8. \qquad 390.$$

To 10 gms. (1 mol.) of mannitol dissolved in 500 c.cs. of pyridine, 50 gms. (excess) of benzoyl chloride are slowly added in the warm, the whole allowed to stand overnight and poured into 1 litre of cold 10% sulphuric acid. The ester is filtered off at the pump, washed with cold water and recrystallised from alcohol.

$$\begin{matrix} CH_2OH \\ (\dot{C}HOH)_4 \\ \dot{C}H_2OH \end{matrix} + 2C_6H_5COCl \xrightarrow{C_5H_5N} \begin{matrix} CH_2O.OC.C_6H_5 \\ (\dot{C}HOH)_4 \\ \dot{C}H_2O.OC.C_6H_5 \end{matrix} + 2HCl.$$

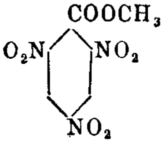
*Yield.*—80% theoretical (17 gms.). Colourless needles; insoluble in water; M.P. 178°. (A., 301, 102.)

Ethyl acetate can be prepared in a like manner.

**Reaction CVII. Action of an Alkyl Iodide on the Silver Salt of an Acid.** (J. C. S., 67, 600.)—This method is used when an ester is not easily obtained by the usual methods owing to steric hindrance or some such cause. The silver salt and alkyl iodide are heated or shaken together with or without an inert solvent, benzene, etc. The precipitated silver halide is filtered off, and the ester separated from the filtrate by distillation or some other method.

$$R_1I + RCOOAg = R.COO.R_1 + AgI.$$

PREPARATION 215.—**Methyl Trinitrobenzoate** (*Methyl ester of* s-*trinitrobenzoic acid*).



$$C_8H_5O_8N_3. \qquad 271.$$

10 gms. (1 mol.) of *s*-trinitrobenzoic acid are treated with 14 gms. (1 mol. $NH_4OH$) of 10% (D. 0·959) ammonium hydroxide solution, slight excess of aqueous silver nitrate solution added, and the precipitate filtered at the pump, washed with cold water and dried as described on p. 484. The dried silver salt and 20 gms. (excess) of methyl iodide are refluxed on a water bath for 1 hour, excess of methyl iodide is distilled off, and the residue extracted with boiling alcohol and filtered. The filtrate is concentrated to small bulk, cooled, and the precipitate recrystallised from alcohol.

$$C_6H_2(NO_2)_3(COOAg)[2:4:6:1] + CH_3I =$$
$$C_6H_2(NO_2)_3(COOCH_3)[2:4:6:1] + AgI.$$

*Yield.*—80% theoretical (8 gms.). Colourless crystals; insoluble in water; M.P. 157°. (J. C. S., 67, 600.)

**Reaction CVIII. Polymerisation of an Aldehyde to an Ester.** (B., 20, 647.)—In the presence of sodium benzylate 2 mols. of benzaldehyde polymerise to yield benzyl benzoate. The reaction is peculiar to aromatic aldehydes.

$$C_6H_5.CH_2.ONa + \begin{array}{l} O : CHC_6H_5 \\ \\ O : CHC_6H_5 \end{array} \rightarrow C_6H_5.C\begin{array}{l} /\ OCH_2C_6H_5 \\ -\ O\ .\ Na \\ \backslash\ OCH_2C_6H_5 \end{array}$$

$$\rightarrow C_6H_5CH_2.O.COC_6H_5 + NaOCH_2C_6H_5.$$

The reaction should be compared with the simultaneous oxidation and reduction of aromatic aldehydes under the influence of concentrated caustic alkali (Reaction LXIII.).

PREPARATION 216.—**Benzyl Benzoate** [*Benzyl ester of phenylmethan acid*].

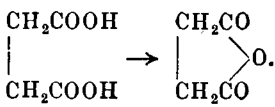
$$C_6H_5CO.O.CH_2C_6H_5. \qquad C_{14}H_{12}O_2. \qquad 212.$$

A solution of 0·75 gm. of sodium in 18 gms. of benzyl alcohol (previously dried over potassium hydroxide and redistilled) is heated on a water bath using a calcium chloride tube on the flask, and added to 75 gms. (2 mols.) of benzaldehyde (previously dried over calcium chloride and distilled in a current of carbon dioxide). The whole is heated on a water bath for 20 hours, and acidified with 5 c.cs. of glacial acetic acid. Water is added, and the oil which separates dried over calcium chloride and distilled in a high-temperature distilling flask (see p. 19). Some unchanged benzaldehyde comes over; the fraction 320°—326° is retained.

$$2C_6H_5.CHO \xrightarrow{C_6H_5CH_2ONa} C_6H_5.CH_2.O.CO.C_6H_5.$$

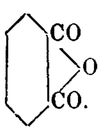
*Yield.*—80% theoretical (60 gms.). Colourless crystals; insoluble in water; M.P. 20°; B.P. 323°. (B., 20, 649; O. S., II., 5.)

**Reaction CIX. Action of Heat on certain Dibasic Acids.** (B., 10, 326.)—When acids such as phthalic acid or succinic acid, which contain two carboxyl groups attached to adjacent carbons, are heated, they readily lose water and pass into the acid anhydride.



Dibasic acids with the carboxyl groups not attached to adjacent carbons only form anhydrides with difficulty or not at all.

PREPARATION 217.—**Phthalic Anhydride** (*Anhydride of* 1 : 2-*benzene-dicarboxylic acid*).



$$C_8H_4O_3. \qquad 148.$$

20 gms. (1 mol.) of phthalic acid (Preparation 187) are sublimed over a naked flame in the apparatus described on p. 31. Long needles collect on the filter paper and funnel.

$$C_6H_4(COOH)_2[1:2] \rightarrow C_6H_4(CO)_2O[1:2].$$

*Yield.*—Almost theoretical (18 gms.). Colourless needles; yields phthalic acid with water; M.P. 128°; B.P. 284°. (B., 10, 326.) For catalytic oxidation of naphthalene, see J. S. C. I., 51, 159.

Succinic anhydride (see Preparation 220) can be similarly prepared.

The following reactions, unlike the above, deal mostly with the preparation of anhydrides in which the carboxyl groups belong to different molecules:—

**Reaction CX. Action of an Acyl Chloride on the Sodium Salt of an Acid.** (A. Ch., [3], 37, 311.)—This is a standard method of preparing acid anhydrides. By using the sodium salt of one acid with the acid chloride of another, mixed anhydrides may be obtained.

$$R_1COONa + Cl.CO.R_{11} = R_1CO.O.COR_{11} + NaCl.$$

Simple anhydrides can also be prepared by the action of the alkali salt of an acid on half the quantity of phosphorus oxychloride necessary for its conversion to the acid chloride which is intermediately formed.

$$2CH_3COONa + POCl_3 = 2CH_3COCl + NaPO_3 + NaCl.$$
$$2CH_3COONa + 2CH_3CO.Cl = 2(CH_3CO)_2O + 2NaCl.$$

This latter method is used industrially.

PREPARATION 218.—**Acetic Anhydride** [*Ethan acid anhydride*].

$$(CH_3CO)_2O. \qquad C_4H_6O_3. \qquad 102.$$

100 gms. (excess) of crystallised sodium acetate are heated on a metal tray or in a porcelain basin until the crystals melt in their own water of crystallisation (p. 509), solidify, and finally remelt. (*Caution!*) When the whole mass has fused (315°), it is allowed to cool and is powdered; overheating must be avoided. It is immediately introduced into a 250-c.c. retort connected by a water condenser to a receiver consisting of a distilling flask, the side tube of which is fitted with a calcium chloride tube connected with the draught pipe. The whole apparatus is fitted up in a fume cupboard. 40 gms. (1 mol.) of acetyl chloride are slowly added by means of a dropping funnel fixed in the tubulus of the retort, which is meantime cooled in water and shaken at intervals. When addition is complete, the dropping funnel is removed, the mixture stirred with a glass rod, and the tubulus closed with a glass stopper. The retort is now heated with a luminous flame, which is constantly moved about, until nothing further distils. Some fused sodium acetate is added to the distillate and the latter redistilled from the receiving flask into another distilling flask fitted with a calcium chloride tube as before. Each time before beginning distillation the air in the apparatus should be displaced by dry air blown into it *viâ* the calcium chloride tube by means of a rubber bulb attachment. This will help in the production of a colourless liquid.

In the second distillation the fraction distilling at 130°—140° is collected separately.

$$CH_3COCl + NaO.CO.CH_3 = (CH_3CO)_2O + NaCl.$$

*Yield.*—80% theoretical (45 gms.). Colourless liquid; suffocating smell; B.P. 138°; D. $^{15}_{4}$ 1·08. (A. Ch., [3], 37, 311.)

*Note.*—If a purer product is desired, distillation over fused sodium acetate must be repeated until a drop of the distillate shaken with a little warm water (*Caution!*) gives no precipitate on addition of dilute nitric acid and silver nitrate. This test shows the complete absence of acetyl chloride. Benzoic anhydride (p. 267), etc., is obtained in similar manner.

For references to thermal "anhydrisation," see A. C. R., 1934, 125.

**Reaction CXI. Action of Dehydrating Agents on a Free Acid.** (B., 34, 186, 2074; A., 226, 8.)—This is a usual method of preparing the anhydrides of acids, the chlorides of which are not readily available. Acetic anhydride is very frequently used—acetyl chloride can also be employed.

$$2R.COOH + (CH_3CO)_2O = (RCO)_2O + 2CH_3COOH.$$

PREPARATION 219.—**Cinnamic Anhydride** [*Anhydride of* 3-*phenyl*-2-*propen acid*].

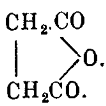
$$(C_6H_5CH : CHCO)_2O. \qquad C_{18}H_{14}O_3. \qquad 278.$$

50 gms. (2 mols.) of dry finely powdered cinnamic acid and 250 gms. (excess) of acetic anhydride are refluxed together for 8 hours, and distilled to 146°. The cold residue is extracted with ether, the extract filtered, and ether removed on a water bath. The residue is recrystallised from alcohol.

$$2C_6H_5CH : CHCOOH \xrightarrow{-\,H_2O} (C_6H_5CH : CHCO)_2O.$$

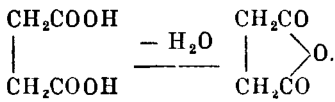
*Yield.*—Almost theoretical (46 gms.). Colourless needles; soluble in ether and in hot alcohol; M.P. 136°. (B., 34, 186, 2074.)

PREPARATION 220.—**Succinic Anhydride** [*Anhydride of butan-diacid*].



$C_4H_4O_3$. 100.

10 gms. (1 mol.) of finely powdered succinic acid are refluxed for 3 hours with 20 gms. (excess) of acetyl chloride and allowed to stand in a soda-lime desiccator until acetyl chloride and acetic acid are completely removed. The residue is recrystallised from absolute alcohol.



*Yield.*—Almost theoretical (9 gms.). Long needles; M.P. 119·6°; B.P.$^{10}$ 131°; B.P.$^{760}$ 261°. (A., 226, 8; O. S., XV., 93.)

**Reaction CXII. Action of certain Bases on Acyl Chlorides.** (B., 34, 2070; J. pr., [2], 50, 479.)—When pyridine or quinoline act on an acid chloride, and the addition product which is formed treated with water, the acid anhydride is obtained (*cf.* Reaction CIX.).

$$2R.CO.Cl \xrightarrow[H_2O]{C_5H_5N} (RCO)_2O + 2HCl.$$

PREPARATION 221.—**Benzoic Anhydride** (*Anhydride of benzenemonocarboxylic acid*).

$(C_6H_5CO)_2O$. $C_{14}H_{10}O_3$. 226.

25 gms. (2 mols.) of benzoyl chloride are slowly added to 20 c.cs. of pyridine and 8 gms. of anhydrous sodium carbonate; after $\frac{1}{2}$ hour the whole is poured into water, the precipitate filtered and washed with cold water, and dried first on a porous plate, and then in a desiccator. It is recrystallised from petroleum ether, which is removed under reduced pressure.

Colourless needles; insoluble in water; M.P. 42°. (J. pr., [2], 50, 479. O. S., III., 21; Rec., 47, 321; E.P., 280,373 (1926).)

The anhydride may also be obtained by the action of acetic anhydride on benzoic acid. (B., 57, 431.)

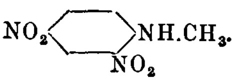
# CHAPTER XVIII

## THE LINKING OF NITROGEN TO CARBON

### Nitro Compounds

**Reaction CXIII. Action of Dilute Nitric Acid on some Organic Compounds.**—Dilute nitric acid, which very often acts as an oxidising agent, can be used for introducing the nitro group, $NO_2$, under certain conditions. For example, phenol can be converted into nitrophenol by 3% nitric acid, while 4% acid converts methyl- and ethyl-acetanilide into the corresponding dinitro derivatives. The nitro group can also be substituted in the side chain by heating, say, toluene with dilute nitric acid under pressure. The reaction, however, is not generally employed, as it is necessary to boil for some hours. Sodium and potassium nitrates in dilute sulphuric acid and solutions of nitric acid in glacial acetic acid, ether, acetone, and acetic anhydride are also used.

PREPARATION 222.—**Dinitromethylaniline** (1-*Methylamino*-2 : 4-*dinitrobenzene*).



$C_7H_7O_4N_3$. 197.

10 gms. methyl acetanilide * are dissolved in 1 litre of dilute nitric acid (D. 1·029), and the solution heated to boiling under a reflux condenser. The liquid instantaneously assumes a brown colour, and after half an hour's heating becomes turbid and a yellow substance begins to separate out. Two hours' heating is, however, necessary to complete the reaction. On cooling, the substance separates out in yellow crystals, which are recrystallised from aqueous alcohol.

$$C_6H_5N.CH_3COCH_3 + 2HNO_3 + H_2O \rightarrow C_6H_3(NO_2)_2NH.CH_3 + CH_3COOH + 2H_2O.$$

M.P. 175°. (B., 18, 1995.)

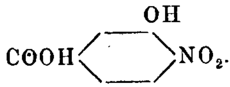
**Reaction CXIV. Action of Concentrated Nitric Acid on Aromatic Compounds.** (B., 20, 333.)—Concentrated nitric acid up to 100% is required for nitrating many compounds which are not oxidised by this treatment. For this reason it is not used in the aliphatic series, nor with compounds containing an easily oxidisable side chain. The reaction is represented by the equation

$$RH + HONO_2 \rightarrow R.NO_2 + H_2O.$$

* Methyl acetanilide is prepared by heating mono-methylaniline with acetyl chloride. It can be purified by recrystallisation or sublimation. M.P. 101°—102°. (B. 10, 328.)

In this reaction the question of temperature is one of importance. In general it should be kept as low as possible to avoid oxidation. When the temperature is raised the tendency to form dinitro, trinitro, and poly-nitro derivatives is much increased.

PREPARATION 223.—**4-Nitro-3-hydroxybenzoic Acid.**




$C_7H_5O_5N$. 183.

50 gms. *m*-hydroxybenzoic acid are dissolved in 175 c.cs. of hot nitro-benzene. The solution is cooled to 35°—40°, and 17 c.cs. fuming nitric acid dissolved in an equal amount of nitrobenzene are slowly added with stirring during 4 hours. The product is filtered, washed with carbon tetrachloride, and crystallised from dilute alcohol.

*Yield.*—15% theoretical (10 gms.). M.P. 227°—228°. (J. C. S., 119, 1428.)

**Reaction CXV. Action of a Mixture of Concentrated Nitric Acid and Concentrated Sulphuric Acid (mixed acid) on Aromatic Compounds.**—This reaction is the most important for nitration and is represented, as before, by the equation—

$$R.H + HONO_2 \longrightarrow R.NO_2 + H_2O.$$

(*a*) The theoretical quantity of nitric acid is added to a large excess of conc. sulphuric acid, and the mixed acid added to the compound to be nitrated. Or the compound may be dissolved in excess of conc. sulphuric acid, and the theoretical quantity of strong nitric acid then added. The excess of sulphuric acid is added to absorb the water formed in the reaction, and which would reduce the concentration of nitric acid ultimately to a point where no nitration would take place. The quantity of sulphuric acid added must be such that its final concentration after nitration, *i.e.*, when it contains the water formed in the reaction plus the water originally present in the nitric acid, must be above a certain minimum, depending on the compound to be nitrated. When this minimum concentration of sulphuric acid is reached nitration again stops.

(*b*) In nitrating bases, the basic group must be protected from oxidation. This may be done in several ways :—

1. By carrying out the nitration in presence of a large excess of conc. $H_2SO_4$. The amine sulphate is first formed, and then nitration takes place.

2. By introducing acyl groups previous to nitration,

$$R.NH_2 \longrightarrow R.NH.COR_1 \longrightarrow R.N(COR_1)_2,$$

where $R_1$ = alkyl or aryl group.

After nitration, the acyl group is split off by hydrolysis.

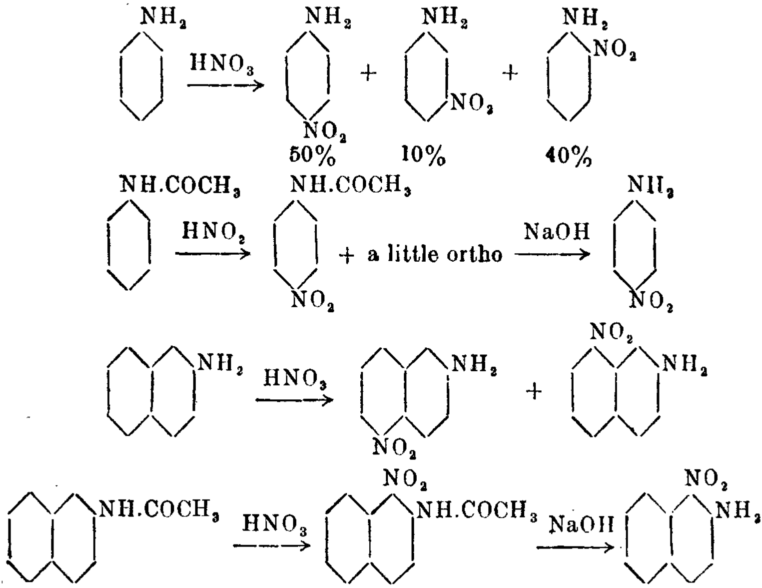
$$NO_2C_6H_4.NH.COR_1 \xrightarrow{H_2O} NO_2C_6H_4.NH_2 + R_1COOH.$$

3. By combining with benzaldehyde to form a benzylidene derivative,

$$R.NH_2 + OCH.C_6H_5 \longrightarrow R.N = CH.C_6H_5,$$

which can be readily nitrated, and the benzylidene group removed subsequently by hydrolysis.

By these methods usually only one isomer is formed in appreciable quantity, *e.g.*,



(c) Sometimes it is necessary to protect the OH group, and the same acyl groups are introduced. For study of nitration, see J. C. S., 1934, 1357.

**Rules of Nitration.**—As a general rule, nitrations should be carried out at as low a temperature as possible, to reduce losses due to oxidation.

The number of nitro groups introduced into the nucleus is dependent on the amount and concentration of the nitric acid, temperature, and duration of nitration.

The position taken by a $NO_2$ group on entering the nucleus depends on the group or groups already present. In general, OH, $NH_2$, Cl, Br, I, $CH_3$, and $CH_2Cl$, are *o*- and *p*- directing, and their presence facilitates the introduction of the nitro group, while $SO_3H$, COOH, CN, CHO, CO, and $NO_2$ are *m*-directing, and tend to retard nitration.

The proportion of isomers formed is not altered to any great extent by temperature.

For a discussion on the different theories of substitution, see Ann. Rep., 1926, 129 ; 1927, 148 ; 1930, 130 ; 1931, 115 ; and Rec., 48, 797.

**Analysis of a Mixed Acid.**—1. *Total Acidity* (calculated as $H_2SO_4$).—About 5 c.cs. of mixed acid are put into a tared weighing bottle and its weight found. This is then washed into a beaker and titrated with N/1 caustic soda solution, using methyl orange as indicator.

$$\% \; H_2SO_4 = \frac{4{\cdot}9 \times \text{c.cs. of NaOH}}{\text{weight taken}}.$$

2. **$H_2SO_4$** (*Actual*).—About 5 c.cs. are weighed out into a tared dish, and heated on a water bath till all the $HNO_3$ and HCl (if any) are driven off. This is then washed into a flask and titrated, as in 1.

$$\text{Total acidity as } H_2SO_4 - \left(HNO_3 \times \frac{49}{63}\right) = \text{real } H_2SO_4.$$

It is better, however, to estimate $HNO_3$ as in 3.

3. **$HNO_3$** *by Nitrometer*.—About 5 gms. of mixed acid are weighed out and placed in the funnel of a nitrometer, and washed in with a little pure conc. $H_2SO_4$. The nitrometer is well shaken until all the NO is evolved. It is then allowed to stand till room temperature is reached, when the temperature and barometric pressure are noted.

The volume of NO at N.T.P. is then calculated.

$$\text{This volume} \times \frac{63}{22400} = \text{weight of } HNO_3 = x.$$

$$\%\ HNO_3 = \frac{x}{\text{weight taken}} \times 100.$$

This figure includes $HNO_2$, which also gives NO in the nitrometer. It can be estimated as in 4.

4. **$HNO_2$** (*Small Amounts*).—5 c.cs. N/10 permanganate solution are diluted with distilled water to 100 c.cs. The mixed acid is then run in from a burette until the $KMnO_4$ is decolorised. The weight of mixed acid is calculated from its specific gravity.

$$HNO_3 \text{ by nitrometer} - \left(HNO_2 \times \frac{63}{47}\right) = \text{real } HNO_3$$

$$1 \text{ mol. } KMnO_4 \equiv 5 \text{ mols. } HNO_2.$$

**Isolation of Nitro Compounds.**—Nitro compounds in many cases separate in the liquid or solid form from the residual acid (" Waste acid "). Since these are usually somewhat soluble in waste acid a further yield can be obtained by diluting the latter with water. Liquid nitro compounds are isolated in a separating funnel, while solids are removed by filtration. Steam distillation is sometimes adopted as in Preparation 232.

" Waste acid " is often used for nitration after addition of the necessary conc. sulphuric acid or oleum, and nitric acid. (See Preparation 228.)

PREPARATION 224.—**Nitrobenzene.**

$$C_6H_5.NO_2. \qquad 123.$$

100 gms. of benzene are placed in a vessel, which is provided with a good efficient mechanical agitator. A mixed acid is made by taking 140 gms. nitric acid (D. 1·41) and 180 gms. conc. sulphuric acid, and mixing well together. Considerable heat is generated in mixing these acids, and before proceeding further the mixture should be cooled. The benzene should now be agitated briskly, and the mixed acid run in slowly. The temperature rises quickly to about 45°, when the flow of acid is reduced, and, if necessary, cooling water applied to the outside of the nitrating vessel. The acid should now be added at such a speed that, when it is all in, the temperature has risen to

60°. The temperature is kept at 60°—70° until nitration is complete (2 hours).

When nitration is complete the mixture is run into a separator, diluted with water and allowed to settle. After a time the layers are separated, the nitrobenzene being washed with a little dilute sodium carbonate solution.

After settling, the nitrobenzene is run off from the bottom, and freed from water by anhydrous calcium chloride until it is clear. The water and any unchanged benzene may also be removed by distillation. The nitrobenzene is then distilled, distillation being stopped when the contents of the flask turn dark in colour, the fraction 208°—212° being collected. The residue in the flask contains dinitrobenzene.

$$C_6H_6 + HNO_3 \rightarrow C_6H_5NO_2 + H_2O.$$

*Yield.*—85% theoretical (134 gms.). Pale yellow liquid with characteristic smell; M.P. 5·7°; B.P. 210°; D. $^{13}_{4}$ 1·2116; important intermediate for dyestuffs. (A., 12, 305; J. pr., 19, 375.)

PREPARATION 225.—*m*-**Dinitrobenzene.**

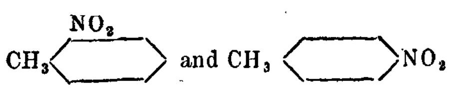
$C_6H_4(NO_2)_2$. 168.

To a mixture of 30 gms. conc. sulphuric acid and 18 gms. of fuming nitric acid, contained in a flask of about 700 c.cs. capacity, 12 gms. of nitrobenzene are gradually adding with shaking. The flask is heated on a water bath in a fume cupboard until a test sample solidifies on pouring into cold water; about 30 minutes' heating is generally required. The contents of the flask are then poured in a thin stream into a large volume of vigorously agitated ice-cold water. The crude dinitrobenzene, which contains about 3% *p*-dinitro and 1% *o*-dinitrobenzene, is filtered off, washed well with water, and recrystallised from alcohol.

$$C_6H_5NO_2 + HNO_3 \rightarrow C_6H_4(NO_2)_2 + H_2O.$$

*Yield.*—75—87% theoretical (12—14 gms.). Pale yellow needles; M.P. 90°. (A., 57, 214.)

PREPARATION 226.—*o*- **and** *p*-**Nitrotoluenes** (1-*Methyl*-2-*nitrobenzene and* 1-*methyl*-4-*nitrobenzene*).




$C_7H_7O_2N$. 137.

100 gms. toluene are placed in a nitrating vessel. A mixed acid, consisting of 150 gms. conc. sulphuric acid and 100 gms. nitric acid (D. 1·44), is cooled and run into the toluene, which is vigorously agitated. The temperature rises to 20°—30°, and is maintained at that, cooling water being passed into the water bath if necessary. After all the acid has been added the temperature is allowed to rise to 50°. This temperature is maintained until the specific gravity of the oil (taken by hydrometer) is 1·15. The oil is then separated from the waste acid in the usual way, washed with water and sodium carbonate solution, and then dried on the water bath.

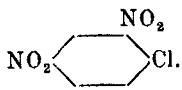
Any unnitrated toluene can be removed by distillation. The *o*-compound may be separated from the *p*-compound by fractional distillation, using a column. 40% of the mixture is distilled off, consisting chiefly of *o*-compound. The *p*-compound is obtained from the residue by cooling at 0°.

If the mixture is cooled to about − 20° (see p. 12) the *p*-compound crystallises out.

The mixture consists of about 65—70% *ortho*-, and about 30% *para*-, with a small percentage of the *meta*-compound.

*Yield.*—Total—almost theoretical (148 gms.). (Z. e., 16, 161; Phil. Mag., 1876, IV.; 1, 17.)

PREPARATION 227.—**1 : 3-Dinitro-4-chlorobenzene.**



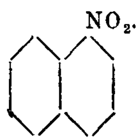
$C_6H_3O_4N_2Cl$. 202·5.

350 gms. of a mixed acid containing 50% nitric acid are placed in a cast-iron pot with good agitation. 113 gms. of chlorobenzene are then run in, the temperature being kept under 5° by external cooling. After all the mixed acid has been added the stirring is maintained for another hour at 5°—10°. The temperature is then slowly raised to 50° and kept at this for 1 hour. 350 gms. conc. sulphuric acid are then dropped in very cautiously with good stirring, and the mixture finally heated up to 115° for half an hour. After cooling, the product is poured into cold water, when it immediately solidifies. The mother liquor is poured off and the dinitrochlorobenzene washed free of acid by heating up in water beyond its melting point (51°) and stirring. The water is then poured off.

*Yield.*—Almost theoretical (200 gms.). Yellow crystals; M.P. 51°.

*Note.*—Care should be exercised that dinitrochlorobenzene is not allowed to touch the skin, as it is liable to produce eczema and sores. (B., 27, 2457; U.S.P., 1220078.) Used in testing for amines.

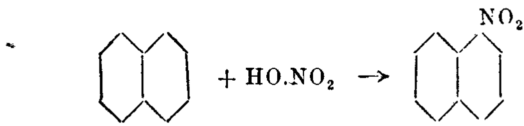
PREPARATION 228.—α-**Nitronaphthalene** (1-*Nitronaphthalene*).



$C_{10}H_7O_2N$. 173.

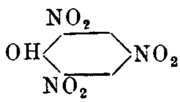
80 gms. nitric acid (D. 1·4) are mixed with 100 gms. conc. $H_2SO_4$ and 300 gms. waste acid from a previous nitration. (In place of waste acid 300 gms. 80% $H_2SO_4$ plus 1 gm. $NaNO_2$ may be used.) The temperature is raised to 40°, and 100 gms. naphthalene, which has been previously melted, is run in gradually with agitation. The temperature is not allowed to rise beyond 50° until all the naphthalene has been added, when it is raised to 60°. The nitro-naphthalene forms a cake on the top of the nitrating vessel as soon as agitation is stopped and cooling is applied. The nitration should be tested every hour after the temperature

has reached 60° by removing part of the cake, which forms on cooling, melting and washing quickly with dilute sodium carbonate solution, removing the alkali and drying with filter paper, and taking the setting point, as described on p. 19. The temperature is maintained at 60° until a setting point 56°—58° is obtained. When nitration is complete agitation is stopped, the nitrating vessel is cooled, and the cake which forms is removed from the waste acid. The cake is then boiled with water to volatilise naphthalene, and some sodium carbonate solution added to remove any adhering acid. The cake is then allowed to solidify, the wash water is run off, and the nitro-naphthalene dried by heating at 120° in an air oven. It may be recrystallised from alcohol.




*Yield.*—90—95% theoretical (111—118 gms.). Yellow needles; M.P. 58·5°; B.P. 304°. (D.R.P., 100417; H. Acta., 15, 236.)

PREPARATION 229.—**Picric Acid** (2 : 4 : 6-*Trinitrophenol*).




$C_6H_3O_7$. 187.

93 gms. phenol are placed in the sulphonating pot and heated to 100°, when 300 gms. 100% sulphuric acid is added, the temperature being kept under 110°, and maintained at this temperature for an hour until sulphonation is complete (test). It is then cooled down to 0°, agitation being maintained.

220 gms. nitric acid (D. 1·5) and 220 gms. 100% sulphuric acid are mixed together and cooled. This is added drop by drop to the sulphonic acid in the pot. It is then allowed to stand overnight at ordinary temperature, and is then very gradually heated up to 30°, and then up to 45°, but no higher.

About 50 c.cs. of the nitrating mixture is then removed from the pot and heated with stirring in a large porcelain basin on a sand bath to 110°—125°. The rest of the mixture is then removed, and is poured gradually into the preheated portion. When all has been added the temperature is kept at 110°—120° for half an hour. 700 c.cs. of water are then added at such a speed that the temperature is kept at 120°. The picric acid separates out on cooling, and is filtered through cotton and washed with water.

*Yield.*—90% theoretical (165 gms.). Yellow powder; explosive; solubility in water at 20°, 1 in 90; M.P. 122·5°. (A., 43, 219; B., 2, 52.)

PREPARATION 230.—(1) *p*-**Nitroacetanilide.**

$NO_2C_6H_4NH.CO.CH_3$. 180.

(2) *p*-**Nitroaniline.**

$NO_2C_6H_4NH_2$. 138.

(1) 20 gms. of finely ground acetanilide are added to 80 gms. conc. sulphuric acid, which is continuously stirred. The solid slowly dissolves, and the temperature, which gradually rises, must not exceed 30°. When all is dissolved the solution is cooled in a freezing mixture to 0°, and a mixed acid, previously cooled, containing 15·5 gms. nitric acid (D. 1·38), and 15 gms. conc. sulphuric acid gradually added during the course of 5 minutes, the temperature not exceeding 3°. When all is added, the solution is allowed to stand for 2 hours or longer, until a sample on pouring into water and boiling with caustic soda gives no odour of aniline. The reaction mixture is poured on to a mixture of 50 gms. of water and 50 gms. of ice, when the nitroacetanilide is precipitated. The precipitate is filtered off and washed with water; it is then stirred with 100 c.cs. of water, sufficient sodium carbonate to render the liquid alkaline to litmus being added, and the whole boiled. By this treatment any *o*-nitroacetanilide present is hydrolysed, but the *p*-compound remains unchanged, and is filtered off at about 50° and washed with water.

*Yield.*—90% theoretical (23 gms.). May be recrystallised from alcohol (M.P. 207°), but is generally used in the crude form for further preparations.

(2) The product derived from the last preparation is stirred with an equal quantity of water, 20 gms. of 35% caustic soda added, and the whole boiled for 2—3 hours. At the end of this time the solution should still show a faint alkaline reaction, and the hydrolysis is complete when a sample dissolves to a clear solution in hydrochloric acid. The liquor is cooled, the *p*-nitroaniline filtered off and washed with a little cold water. It is practically pure, but may be recrystallised from water.

$$C_6H_5NH.COCH_3 + HNO_3 \rightarrow NO_2.C_6H_4.NHCOCH_3 + H_2O.$$
$$NO_2.C_6H_4NH.CO.CH_3 + H_2O \rightarrow NO_2.C_6H_4.NH_2 + CH_3COOH.$$

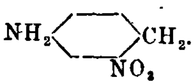
*Yield.*—80% theoretical (15 gms.). Yellow needles; M.P. 147°. (C. Z., 1912, 36, 1055.)

*p*-**Nitroaniline** (*2nd Method*).—18 gms. benzylideneaniline (Prep. 280) are added to 70 gms. of conc. sulphuric acid, the temperature being kept below 50°. The product is cooled to about 5°—10° and maintained at this temperature while a mixture of 11 gms. of nitric acid (D. 1·38) and 11 gms. of conc. sulphuric acid is run in. After standing for 20 minutes the nitration mixture is added to an equal volume of water, and the benzaldehyde removed in a current of steam. The residual liquor is cooled, diluted with water, and neutralised with caustic soda; this causes complete separation, in a very pure form, of the *p*-nitroaniline, which is filtered off, washed with water and dried.

$$C_6H_5N = CH.C_6H_5 + HNO_3 \rightarrow NO_2C_6H_4N = CH.C_6H_5 + H_2O.$$
$$NO_2C_6H_4N = CH.C_6H_5 + H_2O \rightarrow NO_2C_6H_4NH_2 + C_6H_5CHO.$$

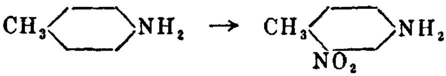
*Yield.*—90% theoretical (12 gms.). (D.R.P., 72173.)

PREPARATION 231.—*m*-**Nitrotoluidine** (2-*Nitro*-4-*aminotoluene*).



$C_7H_8O_2N_2$. 152.

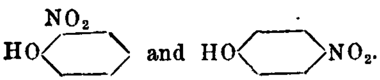
10 gms. *p*-toluidine are dissolved in 200 gms. conc. sulphuric acid. The solution is cooled by a freezing mixture to just below 0°. A mixture of 7·5 gms. nitric acid (D. 1·48) and 30 gms. conc. sulphuric acid is allowed to flow into the well-stirred solution, the temperature being maintained at 0°. When all the mixed acid has been added the mixture is allowed to stand for a short time and is then poured into 500 c.cs. of ice-cold water, the temperature being kept below 25° by the addition of more ice if necessary. The solution is now filtered from impurity and diluted to 3 times its bulk and neutralised with solid sodium carbonate, the temperature being kept as low as possible. The precipitate is then filtered off, pressed dry and finally recrystallised from alcohol.



*Yield.*—65—70% theoretical (10 gms.). Yellow monoclinic needles; M.P. 77·5°. (B., 17, 263.)

**Reaction CXVI. Action of Nascent Nitric Acid on Aromatic Compounds in presence of Concentrated Sulphuric Acid.**—This reaction gives nitro compounds which, in many cases, are only obtained with difficulty by the action of mixed acid. Sodium or potassium nitrate is usually added to the solution of the compound in conc. sulphuric acid. It is usually necessary to keep the temperature below ordinary room temperature.

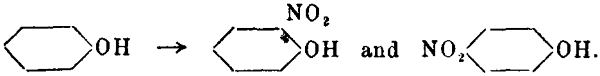
PREPARATION 232.—*o*- **and** *p*-**Nitrophenols** (1-*Hydroxy*-2- and -4-*nitrobenzenes*).



$C_6H_5O_3N$. 139.

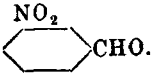
20 c.cs. of water are added to 94 gms. of phenol, and this mixture is allowed to drop into a solution of 150 gms. sodium nitrate in 400 c.cs. water and 250 gms. conc. sulphuric acid. The agitation must be good and during the addition the temperature must be kept at 15°—20°. The stirring is maintained for 2 hours after all has been added. A resinous mixture of nitro bodies is formed from which the supernatant liquor is poured off. The residue is then melted in 500 c.cs. of water and chalk is added with stirring until the mixture is neutral to litmus. This frees the nitro bodies from acid. The wash liquor is poured off and the nitro bodies are distilled in steam, using a wide air condenser. The ortho compound passes over. The residue in the flask is allowed to cool and is then filtered from the mother liquor. The residue which contains the para compound is then boiled up with a litre of 2% hydrochloric acid and filtered through a

hot filter (see p. 11). The para compound crystallises from the hot solution in needles.



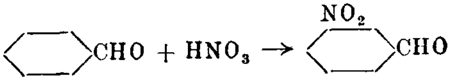

*Yield.*—*Ortho*, 40 gms.; *para*, 40 gms.; total nitrophenol, 60% theoretical; *ortho*, M.P. 44·3°; B.P. 214°; *para*, M.P. 114°; decomposes on boiling. (A., 103, 347; 110, 150; J. C. S., 1931, A., 212.)

PREPARATION 233.—*m*-**Nitrobenzaldehyde.**



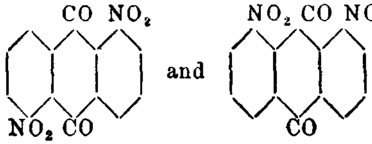

$C_7H_5O_3N$. 151.

100 gms. benzaldehyde are added to a cooled solution of 85 gms. of sodium nitrate in 200 gms. of conc. sulphuric acid. The temperature is not allowed to rise above 30°—35°. The smell of benzaldehyde disappears after the nitration is complete. The mixture is poured into ice, the oily layer separated and washed with warm water, and then with dilute caustic soda solution, and again separated. The oil is cooled (p. 12) to 10° and stirred until the *m*-nitrobenzaldehyde separates. It is then pressed to remove the *o*-compound.




*Yield.*—100 gms. *meta*, 25 gms. *ortho*; 90% theoretical; M.P. *o*- 46°, *m*- 58°. (B., 14, 2802; U.S.P., 1509412.)

PREPARATION 234.—**1 : 5- and 1 : 8 - Dinitroanthraquinone.**

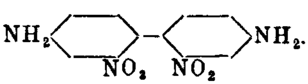



$C_{14}H_6O_6N_2$. 298.

10 gms. anthraquinone are dissolved in 100 gms. conc. sulphuric acid; 10 gms. sodium nitrate (dry) are added with agitation. The mixture is kept at 60°—80° for 12 hours. It is then poured into water and the 1·5- and 1·8-compounds, along with any unchanged anthraquinone, separated and washed. The 1 : 5- is separated from the 1 : 8- by using alcohol or monohydrate (p. 309) as a solvent.

*Yield.*—Almost theoretical; M.P. 1 : 5- above 330°; 1 : 8- above 312°. (B., 16, 363; J. C. S., 1932, 83.)

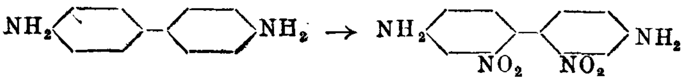
PREPARATION 235.—**2 : 2′-Dinitrobenzidine.**




$C_{12}H_{10}O_4N_4$. 274.

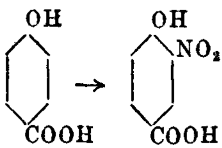
To 56 gms. of pure benzidine sulphate 600 gms. of pure conc. sulphuric acid are added and the mixture well stirred. Solution is completed by

heating up to 60° if necessary. The solution is cooled down to about 10°, but not lower, and 40 gms. potassium nitrate slowly added. After several hours' stirring the solution is poured into about 2 litres of cold water and the dinitrobenzidine sulphate, which is precipitated, filtered off and washed with a little water. The sulphate is then made into a cream with hot water and caustic soda solution added until an alkaline reaction is given to phenolphthalein. The free base is then filtered off, washed with water, and recrystallised from water or from alcohol.



Yellow leaflets, M.P. 214°. (B., 23, 795.)

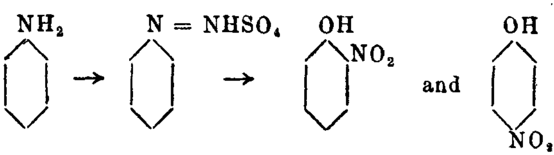
**Reaction CXVII. Action of Nitrous Fumes on certain Organic Compounds.**—The nitro group, $NO_2$, can be introduced in some cases by the action of nitrous fumes, the nitrous fumes being passed through the solution in glacial acetic acid. Sodium nitrite in acid solution may also be used, and in this reaction gives good yields with amines and phenols, the amines passing through the diazo stage into phenols, *e.g.*,



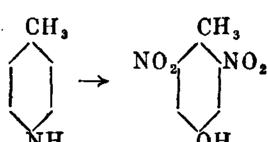
(90 % yield).

The nitrous acid in the reaction is oxidised to nitric acid, and this produces nitration.

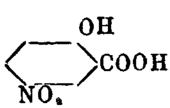
$$3HNO_2 \rightarrow HNO_3 + 2NO + H_2O.$$



When the *p*-position is occupied, the yield is almost theoretical, *e.g.*,



PREPARATION 236.—***m*-Nitrosalicylic Acid.**



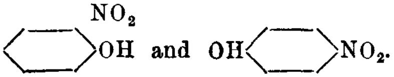
$C_7H_5O_5N$. 183.

100 gms. salicylic acid and 130 gms. sodium nitrite are mixed with 150 c.cs. water and 1,200 c.cs. sulphuric acid (D. 1·52) are slowly added, the

temperature being kept at 10°—15°. After 4 hours the mixture is warmed to 50° and then set aside till the evolution of nitrous fumes ceases. The mass is then warmed on the water bath. On cooling, crystals of *m*-nitrosalicylic acid separate out, and are filtered off, washed and recrystallised twice from water.

*Yield.*—64% theoretical (78 gms.). Needles; M.P. 228°. (J. pr., [11], 42, 550.)

PREPARATION 237.—*o*- **and** *p*-**Nitrophenols.**




$C_6H_5O_3N$. 139.

10 gms. aniline are dissolved in 100 c.cs. of 25% sulphuric acid and the solution cooled to 15°. 300 gms. sodium nitrite are dissolved in 100 c.cs. water and this solution added in two portions. When the first third is added cooling is applied, and the remainder of the nitrite is added without cooling. The mixture is then poured into a large evaporating basin on a water bath and boiling 50% sulphuric acid is cautiously added. When the action is over, the whole is steam distilled when the *o*-nitrophenol passes over. The *p*-compound is then extracted from the residue as in Preparation 232.

*Yield.*—*o*-Compound (4·7 gms.), *p*-compound (3·3 gms.), total 53% theoretical (see p. 276). (J. pr., 148, 298.)

**Reaction CXVIII. Action of Nitrous Acid on Aromatic Amines in presence of Cuprous Salts** (Sandmeyer).

$$R.NH_2 \longrightarrow R.NO_2.$$

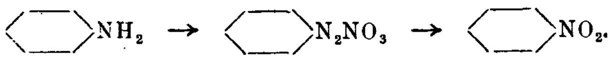
For other examples and a discussion of the Sandmeyer reaction, see pp. 154, 345.

PREPARATION 238.—**Nitrobenzene.**

$C_6H_5NO_2$. 123.

9 gms. aniline are mixed with 50 c.cs. water and 20 gms. conc. nitric acid (D. 1·4). The solution is cooled to 0°—5° and 15 gms. sodium nitrite in 50 c.cs. water added. The mixture is then poured into a flask containing the cuprous salt, prepared by dissolving 50 gms. cupric sulphate and 15 gms. grape sugar in 100 c.cs. water, and adding 20 gms. caustic soda in 60 c.cs. water to the boiling solution; the mixture is shaken till all the copper is reduced, and is then rapidly cooled, and finally acidified by a slight excess of acetic acid.

The combined mixtures are allowed to stand for 1 hour, or until the evolution of nitrogen ceases. The nitrobenzene is then separated by steam distillation.




*Yield.*—50% theoretical (5 gms.). Yellow liquid; M.P. 5·7°; B.P. 210°. (B., 20, 1494.)

## Reaction CXIX. Action of Silver Nitrite on Alkyl Halides.

$$R.I + AgNO_2 \longrightarrow R.NO_2 + AgI.$$

This is an important method of preparing aliphatic nitro compounds.

PREPARATION 239.—**Nitromethane.**

$$CH_3NO_2. \qquad CH_3O_2N. \qquad 61.$$

44 gms. (slight excess) of dry silver nitrite (see p. 517) are mixed with an equal bulk of dry sand and placed in a reflux apparatus; 41 gms. (1 mol.) of methyl iodide are gradually added, and the whole heated on a water bath for 2 hours. The mixture is then distilled from a water bath, the fraction 95°—101° being separately collected. It is redistilled over silver nitrite to remove the last traces of iodide.

$$CH_3I + AgNO_2 \longrightarrow AgI + CH_3NO_2.$$

Heavy, inert, insoluble, colourless liquid; B.P. 101°; D. $^4_4$ 1·1580. (A., 171, 18; O. S., IX., 92.)

Nitromethane can also be prepared by the action of sodium or potassium nitrite on the corresponding salt of monochloroacetic acid. (O. S., III., 83.)

$$ClCH_2COONa + NaNO_2 \longrightarrow NO_2CH_2COONa + NaCl$$
$$NO_2CH_2COONa + H_2O \longrightarrow NO_2CH_3 + NaHCO_3.$$

PREPARATION 240.—**Nitroethane.**

$$C_2H_5.NO_2. \qquad C_2H_5O_2N. \qquad 75.$$

By-product.—**Ethyl Nitrite** (*Ethyl ester of nitrous acid*).

$$C_2H_5.O.NO. \qquad C_2H_5O_2N. \qquad 75.$$

42 gms. (a slight excess) of dry silver nitrite (see p. 509) are placed in a round-bottomed flask fitted with a reflux condenser. To recover the by-product (ethyl nitrite), ice-water must be used in the condenser, which should be a long one. 34 gms. (1 mol.) of ethyl iodide are added, gradually, through the condenser tube, so that the liquid boils vigorously but not too violently. The flask must not be disturbed during the process, for it is important that the silver nitrite should be gradually penetrated by the iodide. The flask is then warmed for 2 hours on a water bath, well cooled, fitted to a distillation apparatus, and the contents fractionally distilled. Ethyl nitrite distils over at 68°, and is collected in the same way as ether (see p. 20) in a flask cooled in a good freezing mixture. The temperature then rises and the second fraction, nitroethane, is collected at 110°—114° and redistilled.

$$C_2H_5I + AgNO_2 \begin{array}{l} \longrightarrow C_2H_5NO_2 + AgI. \\ \longrightarrow C_2H_5ONO + AgI. \end{array}$$

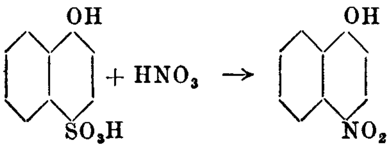
*Yield.—Nitroethane*: 50% theoretical (8—9 gms.). Colourless liquid; insoluble in water; B.P. 113°—114°; D. $^{13}_4$ 1·058.

*Yield.—Ethyl nitrite*: 50% theoretical (8—9 gms.). Volatile liquid; oppressive odour; resembling that of apples when dilute; B.P. 17°; D. $^{15·5}_4$ 0·947. (A., 171, 18.)

**Reaction CXX. Action of Concentrated Nitric Acid on certain Sulphonic Acids.**

$$R.SO_3H + HNO_3 \rightarrow R.NO_2.$$

This reaction goes easily in the anthraquinone series, but only in the naphthalene series when the $SO_3H$ is in the $\alpha$-position.




In the process of nitration with mixed acid, in many cases a sulphonic acid is formed in the first instance, the sulphonic group being ultimately replaced by the $NO_2$ group.

**Reaction CXXI. Action of Tetranitromethane on Bases.** (B., 1920, 53, 1529.)—The tetranitromethane is decomposed by weak bases in alcohol or acetone solution into nitroform and nitric acid.

$$C(NO_2)_4 + H_2O \rightarrow HC(NO_2)_3 + HNO_3,$$

the base becoming nitrated during the process.

Tetranitromethane is dangerous. (See B., 46, 2537.)

# CHAPTER XIX

## THE LINKING OF NITROGEN TO CARBON (*continued*)

**Reaction CXXII. Action of Phenols and Aromatic Amines on Diazonium Compounds.**—Diazonium compounds combine with phenols and aromatic bases to form azo dyestuffs.

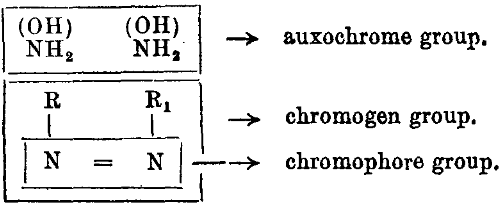
$$\mathrm{R{-}\underset{\underset{\displaystyle N}{|||}}{N}{-}Cl} + \mathrm{H.C_6H_4.\underset{(OH)}{NH_2}} \longrightarrow \mathrm{R.\overset{\displaystyle H}{\dot{N}}.Cl} \atop {\| \atop \mathrm{N.C_6H_4.NH_2\ or\ (OH)}}$$

Intermediate compound.

HCl is split off and an azo colour is formed.

$$\mathrm{R{-}N = N.C_6H_4.NH_2\ or\ (OH).}$$

The process is known as "coupling." R is seldom aliphatic. In the azo compound N is trivalent, while in the diazonium compound N is pentavalent. The diagram shows the name given to the different groups in the azo compound.

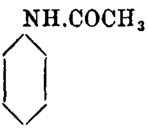



### Laws of Formation of Azo Colours

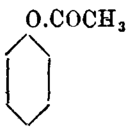
Bases are "coupled" in slightly acid solution, while phenols are "coupled" in slightly alkaline solution.

Coupling usually takes place in the *p*-position to the $NH_2$ or OH group, and, if this is occupied, in the *o*-position, but never in the *m*-position.

If the $NH_2$ or OH groups are substituted by an acetyl group no coupling takes place, *e.g.*,

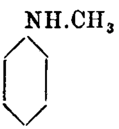



or

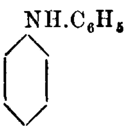



do *not* couple.

If the $NH_2$ is substituted by an alkyl or aryl group coupling takes place, *e.g.*,




and




*do* couple.

If the H in OH is replaced by any group, no coupling takes place.

When both an OH and $NH_2$ are present in the azo compound, *e.g.*, H-Acid (the compound which is diazotised is termed the diazo component), and coupling does take place, then the coupling can be carried out in acid or in alkaline solution, taking place in the *ortho*-position to the $NH_2$ in acid solution, and *ortho* to the OH in alkaline solution.

When one azo component is used, the colour is termed a mono-azo colour.

When two azo components are used, *e.g.*, with benzidine, dis-azo-colours are formed, *e.g.*,

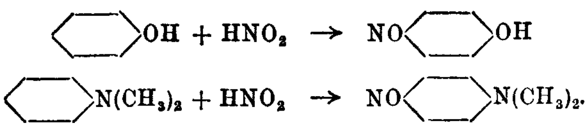
benzidine → salicylic acid.
benzidine → resorcinol.

benzidine → salicylic acid.
benzidine → α-naphthylamine ] → N.W. acid (Trisazo colour).

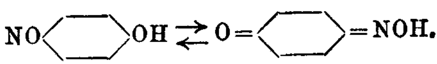
The sign → being used to indicate " coupled to."

For examples, see section on Dyes, etc.

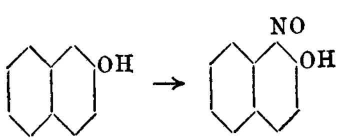
**Reaction CXXIII. Action of Nitrous Acid on Phenols, and Tertiary Aromatic Amines.** (A., 277, 85.)

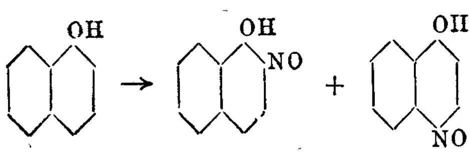


The nitrous acid is usually generated by the action of sodium nitrite on an acid solution. The nitrosophenols are identical with the quinone monoximes, formed by acting on quinone with hydroxylamine.

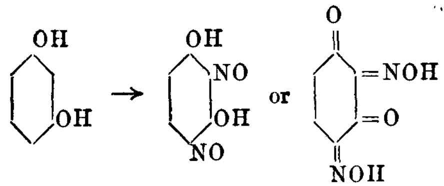


The NO group in the benzene series is introduced in the *para*-position in both cases. In the naphthalene series the β-compound gives the 1-nitroso compound, while the α-compound gives a mixture of the 2- and 4-nitroso compounds. (J. C. S., 1930, 1969.)





Dihydroxy phenols give di-nitroso compounds.

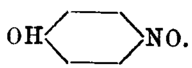


**Resorcinol** **Resorcin green**

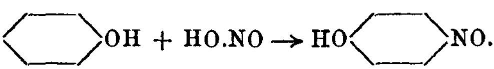
The presence of sodium nitrate in the nitrite used has a harmful effect on the stability of nitroso compounds. This action may be minimised by the addition of reducing agents, *e.g.*, sodium metabisulphite. (J. Soc. Dyer., 41, 275.)

Phenyl dialkylamines react with nitrous acid to give nitroso compounds, the NO group entering the *p*-position, if this is free, to the basic group. These nitroso compounds, generally blue or green in colour, give yellow or red salts with mineral acids. Purely aromatic tertiary amines, *e.g.*, triphenylamine, do not yield such nitroso compounds.

PREPARATION 241.—*p*-**Nitrosophenol.**

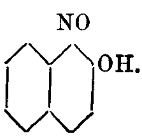
 $C_6H_5O_2N$. **123.**

100 gms. of phenol are dissolved in a solution of 50 gms. of caustic soda, 100 gms. sodium nitrite and 2 litres water. 3 gms. sodium metabisulphite are also added (see above). The temperature is reduced to 7°. 200 c.cs. conc. sulphuric acid are added to 600 c.cs. water, and, when cooled, is gradually run into the solution. The nitrosophenol gradually separates out, and, after stirring for 2 hours, is filtered off and washed with ice-water.



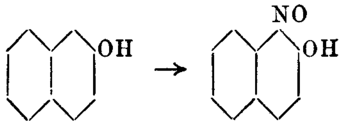
*Yield.*—95% theoretical (124 gms.). Colourless crystals; soluble in hot water, alcohol, and ether; M.P. 126° (with violent decomposition). (A., 277, 85.)

PREPARATION 242.—**Nitroso-β-naphthol** (1-*nitroso*-2-*hydroxynaphthalene*).

 $C_{10}H_7O_2N$. **173.**

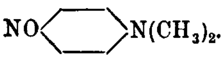
10 gms. β-naphthol are dissolved in 2·8 gms. caustic soda in 100 c.cs. water and made up to 200 c.cs. with water. 5 gms. sodium nitrite dissolved in a little water are carefully added. The mixture is cooled by the addition of 100 gms. ice, and 140 c.cs. 10% sulphuric acid are slowly run in with constant stirring, the temperature being kept below 5°. The nitroso compound separates as a pale yellow precipitate. It is allowed to stand for 2 hours, filtered, and washed with water until the washings

are only slightly acid. It is then dried and crystallised from petroleum ether.



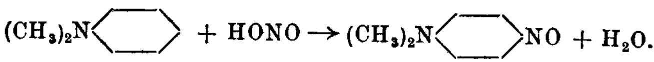
*Yield.*—Almost theoretical (12 gms.). Red needles; M.P. 110°; sparingly soluble in water. (B., 27, 3075; O. S., II., 61; XI., 13.)

PREPARATION 243.—*p*-**Nitrosodimethylaniline.**



$C_8H_{18}ON_2$. **150.**

10 gms. dimethylaniline, dissolved in 26 gms. conc. hydrochloric acid and 50 c.cs. water, are cooled in a freezing mixture. 6 gms. sodium nitrite in 10 c.cs. water are then slowly added with constant stirring. The separation of the hydrochloride of nitrosodimethylaniline soon begins. After standing for ½ hour it is filtered and washed with about 20 c.cs. alcohol, to which 1 or 2 c.cs. hydrochloric acid has been added. The hydrochloride is then made into a paste with water and caustic soda solution added in the cold till alkaline. The yellow colour of the salt changes to the green of the free base. The base is now filtered and the residue well pressed. It may be crystallised from benzene.



*Yield.*—Almost theoretical (12 gms.). Green crystals; M.P. 85°; somewhat volatile in steam; used in preparation of thiazine dyestuffs (p. 387). (B., 7, 810; 8, 616; 12, 523.)

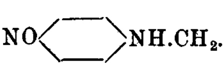
**Reaction CXXIV. Action of Nitrous Acid on Secondary Amines, and subsequent Rearrangement of the Products.**

$$R_2.NH + HO.NO \rightarrow R_2N.NO.$$

The nitrosamines are neutral oily liquids of little importance in themselves. This reaction, however, serves to separate secondary bases from mixtures of primary, secondary and tertiary. The aromatic nitrosamines undergo an interesting rearrangement when heated with alcoholic hydrochloric acid (B., 20, 1247), the nitroso group migrating to a position in the nucleus, forming *p*-nitroso compounds.

$$C_6H_5N(NO)CH_3 \rightarrow NOC_6H_4NH.CH_3.$$

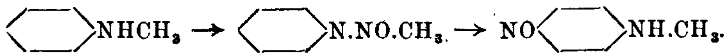
PREPARATION 244.—*p*-**Nitrosomethylaniline.**



$C_7H_8ON_2$. **136.**

10 gms. methylaniline dissolved in 15 c.c. conc. hydrochloric acid and 40 gms. ice are treated with 7 gms. sodium nitrite in 25 c.cs. water.

Methyl-phenyl nitrosamine separates as a yellow oil, which solidifies on cooling (M.P. 12°—15°). 2 gms. methyl-phenyl nitrosamine are dissolved in 4 gms. ether and 8 gms. absolute alcohol which have been saturated with hydrochloric acid gas then added. After a time needles separate out which are filtered and washed with a mixture of alcohol and ether.



*Yield.*—Almost theoretical; M.P. 118°. (B., 19, 2991; O. S., XIII., 82.)

**Reaction CXXV. Action of Alkyl Halides on Phthalimide (Potassium Salt).**—When an alcoholic solution of phthalimide is treated with the theoretical quantity of caustic potash dissolved in alcohol, a crystalline compound—potassium phthalimide—separates out (see p. 427).

$$C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle NH \rightarrow C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle N.K.$$

When this salt is treated with alkyl halide, a derivative of phthalimide is formed.

$$C_4H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle N.K + R.I \rightarrow C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle N.R + KI.$$

The reaction is used chiefly with alkyl halides, although when certain acidic groups are present in the nucleus in the *o*- or *p*-position to the halogen, the reaction gives satisfactory results with aryl halides.

When the phthalimide derivative is hydrolysed, primary amines are formed, so that the reaction is useful for preparing certain aliphatic amines.

$$C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle N.R + 2H_2O \rightarrow C_6H_4\left\langle\begin{matrix}COOH\\COOH\end{matrix}\right. + R.NH_2.$$

A similar reaction can also be used for the preparation of amino acids (B., 22, 426; 34, 454; 39, 534), *e.g.*,

$$C_3H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle NK + ClCH_2COOC_2H_5 \rightarrow C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle N.CH_2COOC_2H_5$$

$$\xrightarrow[(KOH)]{H_2O} C_6H_4\left\langle\begin{matrix}COOH\\CONH.CH_2COOH\end{matrix}\right. \xrightarrow[(HCl)]{H_2O} C_6H_4\left\langle\begin{matrix}COOH\\COOH\end{matrix}\right. + NH_2CH_2COOH.$$

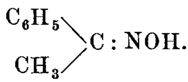
**Reaction CXXVI. Action of Hydroxylamine on Aldehydes and Ketones.**—The majority of aldehydes and ketones react with hydroxylamine, forming oximes.

$$RR_1CO + NH_2OH \rightarrow RR_1C = NOH + H_2O.$$

Hydroxylamine hydrochloride ($NH_2OH.HCl$) is generally used; in most cases the free base is liberated by the subsequent addition of the theoretical quantity of a basic substance (caustic potash, sodium carbonate, etc.). With aldehydes it is advisable to reduce the quantity of

alkali to a minimum, and to warm but gently, if at all. Ketones react much less readily and usually require vigorous heating for 2—3 hours. The reaction is mostly carried out in aqueous-alcoholic solution. The purification of some oximes is best effected by distillation under reduced pressure.

PREPARATION 245.—**Acetophenoneoxime.**



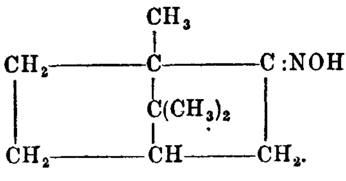
$C_8H_9ON$. 135.

To 5 gms. (1 mol.) of hydroxylamine hydrochloride, dissolved in 10 c.cs. of water and contained in a flask, 3 gms. (less than 1 mol.) of potassium hydroxide dissolved in 5 c.cs. of water are added. 8 gms. (slightly less than 1 mol.) of acetophenone are then added, and the mixture heated in a reflux apparatus on a boiling water bath. Alcohol, in small quantities at a time, is added down the reflux condenser until the boiling solution just becomes clear. After an hour heating is stopped, the solution cooled, and a drop tested with litmus paper. It should be acid owing to the absorption of the hydroxylamine by the ketone. Caustic potash solution is carefully added until the solution is no longer acid. The condenser is again attached, and boiling continued for about 30 minutes, at the end of which time the solution is tested, and, if acid, is neutralised with caustic potash. After about 10 minutes further boiling the solution is once more tested with litmus, and a few drops of it mixed with ice-water. If the test sample solidifies quickly, the reaction is complete, and the contents of the flask are poured into 100 c.cs. of water containing a few lumps of ice. (If the test sample does not solidify, further heating is necessary.) The water should be vigorously stirred during the addition to cause the separation of the oxime in small lumps and flakes. The product is filtered off, washed with water, pressed on a porous plate to dry, and recrystallised from petroleum ether.

$$CH_3.CO.C_6H_5 \rightarrow CH_3.C(:NOH).C_6H_5.$$

*Yield.*—89% theoretical (8 gms.). Colourless needles; M.P. 59°; B.P. $^{760}$ 246° (with decomposition); B.P. $^{20}$ 156°—157° (without decomposition). (B., 15, 2781; J. R. T. C., 1, 340.) *Salicylaldoxime* can be prepared in excellent yield by similar procedure.

PREPARATION 246.—**Camphoroxime** (*Oxime of* d-*camphor*).



$C_{10}H_{17}ON$. 167.

10 gms. (excess) of hydroxylamine hydrochloride, dissolved in the minimum amount of water, are added to 10 gms. (1 mol.) of camphor

dissolved in 150 gms. of 90% alcohol, and the mixture treated with 15 gms. of solid caustic soda. The whole is heated on a water bath, alcohol being added if necessary to keep the camphor in solution, till after about an hour's heating no camphor is precipitated on diluting a test portion of the liquid with an excess of water. The whole liquid is then diluted with a large excess of water, filtered if necessary from a very small precipitate that may come down, and slightly acidified with acetic acid. The precipitated camphoroxime is recrystallised from dilute alcohol.

$$C_9H_{16}CO + H_2NOH = C_9H_{16}C:NOH + H_2O.$$

*Yield.*—75% theoretical (8 gms.). Colourless crystals; M.P. 115°. (B., 22, 605.)

PREPARATION 247.—**Benz*syn*aldoxime** (*α-Benzaldoxime*).

$$\begin{array}{l} C_6H_5C.H \\ \quad\ \ \| \\ \quad\ NOH \end{array} \qquad C_7H_7ON. \qquad 121.$$

14 gms. of caustic soda dissolved in 40 c.cs. of water and 21 gms. of benzaldehyde are mixed in a flask. 14 gms. of hydroxylamine hydrochloride are added in small portions at a time, the mixture being continually shaken. The benzaldehyde gradually disappears, and some heat is developed. On cooling, a crystalline mass separates out. Sufficient water is added to redissolve, and carbon dioxide is passed in until saturated. The oxime then separates, and is extracted with ether; the ethereal solution is dried over anhydrous sodium sulphate. The ether is removed (see p. 36), and the residue distilled under greatly diminished pressure.

$$C_6H_5.CHO + NH_2OH \longrightarrow C_6H_5CH:NOH + H_2O.$$

*Yield.*—50% theoretical (12 gms.). M.P. 35°; B.P.$^{14}$ 123°.

**Reaction CXXVII. Action of Acids, Acid Chlorides, Anhydrides, and Phosphorus Pentachloride on Oximes.** (B., 23, 11; J. C. S., 117, 1045.)—Aldoximes (oximes obtained from aldehydes) exist in two stereoisomeric forms depending on the relative position of the OH group.

$$\begin{array}{c} R.C.H \\ \| \\ N.OH \\ \textit{Syn}\text{-aldoxime } (\alpha). \end{array} \qquad\qquad \begin{array}{c} R.C.H \\ \| \\ OH.N \\ \textit{Anti}\text{-aldoxime } (\beta). \end{array}$$

Both forms yield acetyl derivatives with acetic anhydride. That of the *anti*-oxime decomposes by the action of alkali yielding a nitrile which separates out; whereas that of the *syn*-oxime under the same conditions regenerates the parent form of the oxime which dissolves in the caustic soda used.

$$\begin{array}{c} R.C.H \\ \ddot{N}.OH \end{array} \rightarrow \begin{array}{c} R.C.H \\ \ddot{N}.OCOCH_3 \end{array} \rightarrow \begin{array}{c} R.C.H \\ HO.\ddot{N} \end{array} + CH_3COOH$$

$$\begin{array}{c} R.C.H \\ HO.\ddot{N} \end{array} \rightarrow \begin{array}{c} R.C.H \\ CH_3COO\ddot{N} \end{array} \rightarrow \begin{array}{c} R.C \\ \dddot{N} \end{array} + CH_3COOH.$$

When H is replaced by R no isomerism occurs; but if it is replaced by $R_1$, as in the case of mixed ketones, two isomeric forms exist:

$$\begin{array}{l} R.C.R \\ \quad \ddot{N}.OH \text{ (one form)} \end{array} \qquad\qquad \begin{array}{l} R.C.R_1 \\ \ \ddot{N}.OH \end{array} \text{ and } \begin{array}{l} \ \ R.C.R_1 \\ HO.\ddot{N} \end{array}$$

The one isomer can usually be transformed into the other by heat, exposure to light, or treatment with hydrochloric acid.

*Beckmann Transformation.*—When the *cis* and *trans* forms are treated with certain reagents (especially phosphorus pentachloride) a rearrangement takes place in the molecule. The hydroxyl group interchanges position with the radicle in the *trans* position, and this is followed by a transference of hydrogen from oxygen to nitrogen:

$$\begin{array}{l} \ \ R.C.R_1 \\ HO.\ddot{N} \end{array} \rightarrow \begin{array}{l} R.C.OH \\ \ \ddot{N}.R_1 \end{array} \rightarrow \begin{array}{l} R.C:O \\ \ \dot{N}HR_1 \end{array}$$

$$\begin{array}{l} R.C.R_1 \\ \ddot{N}.OH \end{array} \rightarrow \begin{array}{l} HO.C.R_1 \\ \ \ R.\ddot{N} \end{array} \rightarrow \begin{array}{l} O:C.R_1 \\ RH\dot{N} \end{array}$$

so that substituted amides are formed.

$$e.g., \quad \begin{array}{l} C_6H_5C.C_6H_4CH_3 \\ \quad\ \ \| \\ \ \ HO.N \end{array} \longrightarrow C_6H_5CO.NH.C_6H_4CH_3.$$

oxime of phenyl *p*-tolyl ketone.     benzo-*p*-toluidide.

$$\begin{array}{l} C_6H_5C.C_6H_4CH_3 \\ \quad\ \ \| \\ \quad\ \ N.OH \end{array} \longrightarrow C_6H_5NH.CO.C_6H_4CH_3.$$

anilide of *p*-toluic acid.

The configuration of the oxime can be determined by an examination of the transformation product. (See Ann. Rep., 1924, 111; Brit. Assoc., 1932, (Mills), and Chem. Reviews, 1933, 215.)

PREPARATION 248.—**Transformation of Acetophenoneoxime** (Beckmann). 5 gms. acetophenoneoxime are dissolved in 60 c.cs. of ether, which has been dried over metallic sodium and redistilled, and to this solution is gradually added 7—8 gms. of powdered phosphorus pentachloride. The ether is then removed by distillation. To the residue after cooling are added slowly 25 c.cs. of water. The acetanilide is then filtered off and recrystallised from water, when its melting point is taken.

| | M.P. |
|---|---|
| Acetophenoneoxime . . . . . | 59° |
| Acetanilide . . . . . . . | 112° |

$$\begin{array}{l} CH_3C.C_6H_5 \\ \quad\ \ \| \\ HO.N \end{array} \longrightarrow \begin{array}{l} CH_3CO \\ \quad \vert \\ \ \ NH.C_6H_5 \end{array}$$

**Reaction CXXVIII. Action of Phenylhydrazine, etc., on Aldehydes and Ketones.**—Phenylhydrazones of aldehydes and ketones are generally formed by warming these substances in aqueous-alcoholic solution with phenylhydrazine, phenylhydrazine acetate or phenylhydrazine hydrochloride in presence of excess sodium acetate. Derivatives of phenylhydrazine (*e.g.*, *p*-nitro-phenylhydrazine) also react in a similar manner.

$\alpha$-Hydroxy-aldehydes and $\alpha$-hydroxy-ketones can react with 3 mols. of phenylhydrazine in the following manner :—

$$—CHOH.CHO + H_2N.NH.C_6H_5 \rightarrow —CHOH.\,CH = N.NH.C_6H_5 + H_2O.$$
$$—CH.OH.CH = N.NH.C_6H_5 + NH_2.NH.C_6H_5 \rightarrow$$
$$—CO.CH = N.NH.C_6H_5 + NH_3 + C_6H_5NH_2.$$
$$—CO.CH = N.NH.C_6H_5 + NH_2.NH.C_6H_5 \rightarrow \begin{array}{l} —C.CH = N.NH.C_6H_5 \\ \quad \| \\ N.NH.C_6H_5 \end{array} + H_2O.$$

Many of the simpler sugars react after this manner, forming osazones, which have characteristic appearances under the microscope, and are of special value for identification purposes. (J. C. S., 125, 222.)

PREPARATION 249.—**Glucosazone.**

$$C_4H_5(OH)_4.C(:NNH.C_6H_5).CH.N.NHC_6H_5. \qquad C_{18}H_{22}N_4O_4. \qquad 358.$$

2 gms. of glucose are dissolved in 10 c.cs. water and a solution of 4 gms. phenylhydrazine in 4 gms. glacial acetic acid and 10 c.cs. water is added. The mixture is heated on the water bath for 90 minutes, when the yellow osazone separates out. It is filtered, washed with water, and recrystallised from alcohol.

*Yield.*—2 Gms. golden-yellow needles; M.P. 204°. (B., 17, 579; 20, 821.)

PREPARATION 250.—**Acetonephenylhydrazone** [*Propanon-phenylhydrazone*].

$$(CH_3)_2C = N.NHC_6H_5. \qquad C_9H_{12}N_2. \qquad 148.$$

1 volume of glacial acetic acid is added to phenylhydrazine (1 mol.). The solution is diluted with 2 volumes of water, and acetone (1 mol.) is added. The acetonephenylhydrazone which separates is extracted with ether. The latter is separated, dried over anhydrous potassium carbonate, and distilled under reduced pressure, the fraction 165° at 91 mms. being retained. The oil still contains traces of ammonia, but this may be removed by allowing to stand in a vacuum desiccator over sulphuric acid for a short time.

$$(CH_3)_2CO + H_2N.NH.C_6H_5 \rightarrow (CH_3)_2C = N.NH.C_6H_5 + H_2O.$$

*Yield.*—Theoretical. Colourless, somewhat unstable oil; B.P. $^{91}$ 165°. (B., 16, 662.)

PREPARATION 251.—**Phenylhydrazone of Pyruvic Acid** [*Propanon-acid-phenylhydrazone*].

$$\begin{array}{l} CH_3C : N.NHC_6H_5. \\ \quad | \\ \quad COOH. \end{array} \qquad C_9H_{10}O_2N_2. \qquad 178.$$

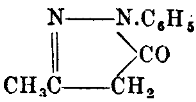
5 gms. (2 mols.) of phenylhydrazine are dissolved in 5 gms. (excess) of glacial acetic acid and 5 c.cs. of water added. 2 gms. (1 mol.) of pyruvic acid are added, and the mixture shaken. The precipitate, after filtration, is washed with dilute acetic acid. It may be recrystallised from alcohol.

$$CH_3.CO.COOH + H_2N.NH.C_6H_5 = CH_3.C:(N.NHC_6H_5)COOH + H_2O.$$

*Yield.*—Theoretical (4 gms.). Yellow needles ; M.P. 192° (the substance must be heated quickly, as it decomposes somewhat below its melting point). (J. pr., [2], 52, 39 ; B., 16, 2241.)

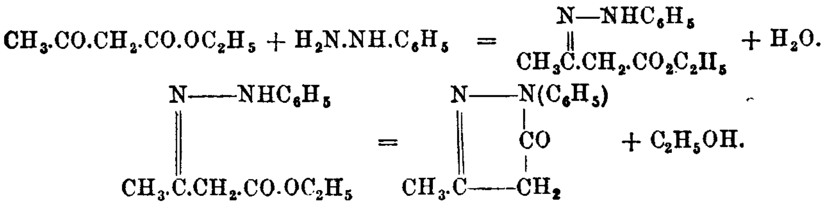
The following modification of the reaction is of interest :—

PREPARATION 252.—**1-Phenyl-3-methylpyrazolone.**



$C_{10}H_{10}ON_2$ 174.

13·5 gms. of ethyl acetoacetate are added to 10 gms. of phenylhydrazine and vigorously shaken. The oil thus obtained is removed and heated on the water bath for about 2 hours until a test portion solidifies when treated with ether. A little ether is poured into the warm liquid, the white crystals which separate being washed with ether and dried at 100°. The product is recrystallised from hot water or alcohol.



*Yield.*—Theoretical (16 gms.). White crystals ; almost insoluble in cold water, ether, and ligroin ; fairly soluble in hot water ; easily soluble in alcohol ; M.P. 127°. (B., 16, 2597.)

**Reaction CXXIX. Action of Semicarbazide on Aldehydes and Ketones.**—This gives rise to semicarbazones which are useful for identification purposes since they crystallise well and melt sharply.

$$R.CHO + NH_2.NH.CO.NH_2 \rightarrow R.CH : N.NH.CO.NH_2 + H_2O.$$

The most convenient general procedure consists in dissolving semicarbazide hydrochloride in a small quantity of water and adding this to a solution of the aldehyde or ketone in pyridine, which also serves to combine with the hydrochloric acid liberated (J.R.T.C., 1929, 52). Alternatively, the semicarbazide hydrochloride (1 mol.) may be dissolved in water along with sodium acetate (rather more than 1 mol.) and this mixture treated with an alcoholic solution of the aldehyde or ketone. When the last-mentioned is soluble in water (*e.g.*, acetone) it is not necessary to use alcohol as solvent.

A few compounds, *e.g.*, benzaldehyde, react with semicarbazide hydrochloride in aqueous solution.

The semicarbazide may be prepared from hydrazine sulphate by the actions of sodium carbonate and potassium cyanate according to the scheme :—

$$2NH_2NH_2.H_2SO_4 + Na_2CO_3 \rightarrow (NH_2NH_2)_2.H_2SO_4 + Na_2SO_4 + H_2CO_3$$
$$(NH_2NH_2)_2.H_2SO_4 + 2KCNO \rightarrow 2NH_2CO.NHNH_2 + K_2SO_4.$$

Preparation 253.—**Acetophenonesemicarbazone.**

$C_6H_5C(CH_3) : N.NH.CO.NH_2$. $C_9H_{11}ON_3$. 177.

A solution of 5 gms. of semicarbazide hydrochloride in 5 c.cs. of water is added to 20 c.cs. of cold pyridine containing 5 gms. of acetophenone. The semicarbazone separates almost immediately in a high state of purity. A second crop may be obtained by diluting the mother liquor with water. The product is easily crystallised from aqueous alcohol.

*Yield.*—Almost theoretical. Soluble in alcohol, acetic acid or hot benzene. Sparingly soluble in water. M.P. 198°.

Preparation 254.—**Acetonesemicarbazone.**

$(CH_3)_2C = N.NH.CONH_2$. $C_4H_9ON_3$. 115.

25 gms. of semicarbazide hydrochloride are dissolved in a small quantity of water; to this a solution of 21·8 gms. of potassium acetate in a small quantity of alcohol is added. The mixed solutions are well shaken and cooled in ice in order to precipitate as much of the potassium chloride as possible, and then filtered. To the filtrate 12·9 gms. of acetone are added and the solution allowed to stand overnight. The precipitated acetone semicarbazone is filtered off. If more acetone is added to the filtrate further precipitation occurs. It is then recrystallised from hot alcohol.

$$\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>C{=}O + H_2N.NH.CONH_2 \rightarrow \begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>C{=}N.NH.CONH_2 + H_2O.$$

*Yield.*—95% theoretical (24 gms.). M.P. 188°—189° with decomposition. (A., 283, 19.)

**Reaction CXXX. Formation of Amino Guanidine Derivatives.**—Amino guanidine combines with aldehydes and ketones in the presence of a mineral acid.

$$RR_1CO + \begin{matrix} NH_2.NH \\ NH_2 \end{matrix}\!\!>C : NH \rightarrow RR_1C{=}\begin{matrix} N.NH \\ NH_2 \end{matrix}\!\!>C : NH + H_2O.$$

Many of the resulting compounds form crystalline picrates, and are isolated as such. The compounds with aromatic aldehydes are isolated as difficultly soluble nitrates.

**Reaction CXXXI. Formation of Semioxamazones.**—Semioxamazide, $NH_2.CO.CO.NH.NH_2$, possesses similar properties to semicarbazide, and reacts well with aldehydes, but with ketones the reaction does not seem to be generally applicable.

$$R.CHO + H_2N.NH.CO.CO.HN_2 \rightarrow R.CH : N.NH.CO.CO.NH_2 + H_2O.$$

The aldehydes or ketones and the semioxamazide are weighed in molecular proportions, and when the former are insoluble in water it is best to dissolve them in a small quantity of alcohol. The semioxamazide, dissolved in the minimum quantity of water, is then added and the mixture thoroughly shaken for some time, when a precipitate of the semi-

oxamazone separates. The semioxamazones are usually white powders of definite melting point, sparingly soluble in the usual organic solvents and insoluble in water. (See also J. C. S., 123, 394.)

**Reaction CXXXII. Action of Aliphatic Halogen Compounds on Aliphatic or Aromatic Primary Amines.**—Secondary, tertiary and quarternary compounds may be formed.

$$R.NH_2 \xrightarrow{R_1Cl} R.NHR_1 \xrightarrow{R_1Cl} RN(R_1)_2 \xrightarrow{R_1Cl} RN(R_1)_3Cl.$$

In this way secondary and tertiary amines may be obtained from primary. Quaternary compounds are obtained by prolonged action of an excess of halogen compound on primary amines, or more usually by the action of halogen compound on a tertiary amine.

PREPARATION 255.—**Dimethylbenzylphenylammonium chloride** (*Methchloride of methylbenzylphenyl amine*).

$$N(CH_3)_2CH_2.C_6H_5)(C_6H_5).Cl. \qquad C_{15}H_{16}NCl. \qquad 247{\cdot}5.$$

A mixture of 5 gms. (1 mol.) of dimethylaniline and 5·3 gms. (1 mol.) of benzyl chloride is placed in a basin, which is left in a desiccator at ordinary temperature for 2—3 months. At the end of this time the mass is practically solid; it is pressed out on porous plate, washed with ether and recrystallised from water or alcohol.

$$C_6H_5N(CH_3)_2 + C_6H_5CH_2Cl \longrightarrow N(CH_3)_2(CH_2C_6H_5)(C_6H_5)Cl.$$

*Yield.*—Theoretical (10 gms.). Colourless plates, containing $1H_2O$ of crystallisation; M.P. 110°. (B., 10, 2079.)

PREPARATION 256.—**Trimethyl-β-naphthylammonium iodide** (*Methiodide of dimethyl-β-naphthylamine*).

$$C_{10}H_7N(CH_3)_2I. \qquad C_{13}H_{16}NI. \qquad 313.$$

5 gms. (1 mol.) of β-naphthylamine, 20 gms. (excess) of methyl iodide, and 20 c.cs. water are placed in a flask and boiled under reflux until the amine completely dissolves (about 3 hours). The quaternary compound formed separates out on cooling. It is filtered off, washed sparingly with water, and dried on porous plate.

$$C_{10}H_7NH_2 + 3CH_3I \longrightarrow C_{10}H_7N(CH_3)_3I + 2HI.$$

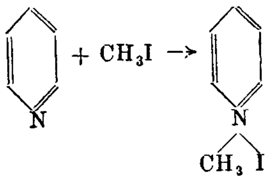
*Yield.*—Theoretical (12 gms.). Colourless needles; decompose when heated or exposed to air. (B., 11, 638; 13, 2054.)

PREPARATION 257.—**Pyridine Methiodide.**

$$C_5H_5NCH_3.I. \qquad C_6H_8NI. \qquad 221.$$

1 c.c. of pyridine and 1 c.c. of methyl iodide are mixed with a glass rod in a small test tube. A vigorous reaction sets in and product becomes very hot. After a few minutes, 5 c.cs. absolute alcohol are added, and

gently warmed to dissolve. On cooling, the product crystallises out in flat needles, which are filtered off and washed with a little alcohol.



M.P. 117°. (B., 3438.)

The following are developments and modifications of the present reaction:

PREPARATION 258.—**Methylaniline** (*Phenylmethylamine*).

$$C_6H_5NH.(CH_3). \qquad C_7H_9N. \qquad 107.$$

20 gms. (1 mol.) of acetanilide (see p. 303), 5 gms. (excess) of sodium wire, and 100 gms. of pure xylene (dried over sodium) are refluxed for 2—3 hours in an oil bath at 130°. After cooling, 15 gms. (rather more than theoretical) of methyl iodide are added, and the mixture digested for a short time until no more methyl iodide condenses in the condenser tube. The xylene is then distilled off.

The methylacetanilide is boiled with concentrated alcoholic potash solution for about 24 hours in a reflux apparatus. The alcohol is distilled off, and the residue neutralised by addition of hydrochloric acid. The residual xylene is then distilled off in steam, the solution made alkaline, and the methylaniline steam distilled. It is taken up with ether, dried over anhydrous sodium sulphate or potassium hydroxide and fractionated.

$$C_6H_5NH.COCH_3 + CH_3I \rightarrow C_6H_5N.(CH_3)CO.CH_3 \rightarrow C_6H_5NH.CH_3.$$

*Yield.*—Theoretical (15 gms.). Yellowish oil; B.P. 192°; D. $^{15}_{4}$ 0·976. (B., 10, 328.)

In certain cases addition of sodium carbonate is effective.

PREPARATION 259.—**Dimethyl-*o*-toluidine.**

$$C_6H_4\begin{cases}N(CH_3)_2\\CH_3.\end{cases} \qquad C_9H_{13}N. \qquad 135.$$

15 gms. *o*-toluidine, 42 gms. methyl iodide and 16 gms. sodium carbonate dissolved in 250 c.cs. water are heated in a reflux apparatus on a water bath for about 2 hours until methyl iodide no longer condenses in the condenser tube. The liquid is then made strongly alkaline with caustic soda solution; the amine is extracted with ether, the extract dried over solid potash and distilled. The amine comes over at 175°—185°.

$$C_6H_4\begin{cases}NH_2\\CH_3\end{cases} + 2CH_3I + Na_2CO_3 \rightarrow C_6H_4\begin{cases}N(CH_3)_2\\CH_3\end{cases} + 2NaI + H_2O + CO_2.$$

*Yield.*—80% theoretical (15 gms.). Pale yellow liquid; B.P. 183°. (B., 24, 563.)

The following preparation is of interest in connection with Fischer's researches on the proteins :—

PREPARATION 260.—**Leucylglycine** [ {4 - *Methyl* - 1 - *oxy* - 2 - *amino* - 1-*pentanyl*} *amino-ethan acid*].

$$\begin{array}{l}(CH_3)_2 : CH.CH_2.CH(NH_2).CO. \\ \qquad\qquad\qquad\quad | \\ \qquad\qquad HOOC.CH_2.NH.\end{array} \qquad C_8H_{16}O_3N_2. \qquad 188.$$

10 gms. (1 mol.) of glycocoll are dissolved in 133 c.cs. (1 mol.) of normal caustic soda, and while cooled with ice and vigorously shaken the solution is treated alternately with 170 c.cs. (excess) of cold N. caustic soda, and 37 gms. (1 mol.) of α-bromoisocaproyl bromide (C., 1910, I., 1345) in four portions, each new addition being made only when the smell of the acid bromide has disappeared. The whole operation lasts about 20 minutes. The liquid is filtered from the small amount of oil it contains, and then treated with 35 c.cs. (excess) of 5N hydrochloric acid. The oil which is precipitated is extracted with ether, and the condensation product precipitated from the ethereal solution after the latter has been concentrated by the addition of a large quantity of petroleum ether. The product α-bromoisocaproylglycine soon crystallises. It is filtered at the pump, washed with petroleum ether, and recrystallised from hot water, or from chloroform.

$$\begin{array}{c}(CH_3)_2 : CHCH_2CHBrCOBr + NH_2CH_2COOH = \\ (CH_3)_2 : CHCH_2CHBr.CO.NH.CH_2COOH + HBr.\end{array}$$

*Yield.*—75% theoretical (26 gms.). Colourless crystals ; M.P. 133°.

The chief fraction of the raw product can also be obtained in crystalline form at once if the alkaline solution is first made slightly acid, treated with a few crystals previously prepared, and then continually stirred while the rest of the hydrochloric acid is slowly poured into it.

The α-bromoisocaproylglycine is converted into leucylglycine by dissolving it in 5 times its weight (excess) of 25% ammonia (D. 0·910), and allowing the solution to stand for 4 days at room temperature. The crystalline paste of ammonium bromide and dipeptide, which is produced when the solution is concentrated on a water bath, is treated with absolute alcohol and again evaporated. The residue is boiled with alcohol, and when cold the leucylglycine, which is insoluble in alcohol, is filtered off at the pump and washed with alcohol until a sample of it dissolved in water gives no further precipitate with silver nitrate. The dipeptide is purified by dissolving it in 15 times its weight of hot water. On cooling, about half the product separates out in crystalline form. By concentrating the mother liquor and precipitating with alcohol, the rest may be obtained. The product should be free from bromine.

$$\begin{array}{c}(CH_3)_2 : CH.CH_2CHBr.CO.NH.CH_2.COOH + 2NH_3 = \\ (CH_3)_2 : CH.CH_2CH(NH_2).CO.NH.CH_2.COOH + NH_4Br.\end{array}$$

*Yield.*—80% theoretical (6 gms. for each 10 gms. of the α-bromoisocaproylglycine taken). Colourless crystals ; soluble in water ; insoluble in alcohol ; M.P. (decomposition) 243°. (B., 42, 3398 ; C., 1909, II., 1546.)

**Reaction CXXXIII. Action of Aromatic Halogen Compounds on Ammonia or Amino Compounds.**—Aliphatic halides readily react with ammonia and amines according to Reaction CXXXII. Aromatic halides are less reactive, unless negative groups are also present. The addition of copper powder or cuprous halide greatly accelerates the elimination of halogen hydride.

In the technical preparations various reagents, *e.g.*, lime and calcium chloride, are added to the catalyst to eliminate corrosion at the high temperatures and pressures required. (E.P., 402063; U.S.P., 1840760.)

PREPARATION 261.—**Diphenylamine** (*Phenylaniline*).

$$C_6H_5NHC_6H_5. \qquad C_{12}H_{11}N. \qquad 169.$$

10 gms. (1 mol.) of acetanilide, 5 gms. of dry potassium carbonate, 20 gms. (excess) of bromo-benzene, and a little cuprous iodide in nitrobenzene solution are refluxed for 15 hours. The dark brown liquid is then steam distilled until no more nitrobenzene passes over. The residue in the distillation flask, consisting of the acetyl derivative of diphenylamine, is a thick brown oil. It is dissolved in ether, filtered, dried over anhydrous sodium sulphate, and the ether removed on a water bath. The residue is crystallised from alcohol, from which it separates as white plates, melting at 102°.

The crystals are dissolved in 30 c.cs. of alcohol, and hydrolysed by boiling with 30 c.cs. of conc. hydrochloric acid for 2—3 hours. The product is distilled in steam, a yellow oil passing over, which solidifies in the condenser.

$$C_6H_5NHCOCH_3 + C_6H_5Br \rightarrow (C_6H_5)_2N.COCH_3 \rightarrow (C_6H_5)_2NH + CH_3COOH.$$

*Yield.*—60% theoretical (7·5 gms.). Yellow plates; soluble in hot alcohol; M.P. 53°; B.P. 310°. (B., 40, 4543.)

PREPARATION 262.—**Phenylglycine-*o*-carboxylic Acid.**

$$C_6H_4\begin{cases} NH.CH_2.COOH \\ COOH. \end{cases} \qquad C_9H_9O_4N. \qquad 195.$$

20 gms. potassium-*o*-chlorobenzoate (prepared from the free acid and caustic potash), 5·5 gms. solid caustic potash, 7 gms. potassium carbonate, 7·5 gms. glycocoll, 15 c.cs. water, and a small quantity of copper powder are placed in a flask provided with a reflux condenser. The mixture is heated to boiling in an oil bath for an hour, the contents finally becoming yellow in colour. The product is cooled somewhat, and boiling water added to redissolve the crystals which have separated. The solution is filtered and the filtrate, while hot, treated with excess of hydrochloric acid; phenylglycine-*o*-carboxylic acid separates, and after some time is filtered off and recrystallised from water.

*Yield.*—Practically theoretical (19 gms.). M.P. 200° (with decomposition). (D.R.P., 142507.)

**Reaction CXXXIV. Action of Silver Cyanide on Alkyl Halides.**

$$RX + AgNC \rightarrow RNC + AgX.$$

Isocyanides (isonitriles or carbylamines) are formed in this reaction.

PREPARATION 263.—**Ethyl*iso*cyanide** (*Ethylcarbylamine*).

$$C_2H_5.NC. \qquad C_3H_5N. \qquad 55.$$

20 gms. (1 mol.) of ethyl iodide are gently refluxed *in a fume cupboard* under a long condenser with 30 gms. (excess) of dry silver cyanide until the liquid ceases to drip back, and the mass is pasty (about 1 hour). A soluble crystalline compound ethyl argento-cyanide, $C_2H_5Ag(NC)_2$, is now contained in the flask. Ethyl isocyanide is formed from it either by heating it to 180°, or better, by heating to 100° with concentrated potassium cyanide solution. A solution of 10 gms. (1 mol.) powdered 98% potassium cyanide in 25 c.cs. of water is added, and the contents of the flask distilled from a water bath in a fume cupboard, the distillate being collected in a flask with an outlet to a good draught pipe. It is redistilled with the same precautions, the fraction 75°—78° being separately collected.

$$C_2H_5I + 2AgNC = C_2H_5Ag(NC)_2 + AgI.$$
$$C_2H_5Ag(NC)_2 + KNC = KAg(NC)_2 + C_2H_5NC.$$

Volatile liquid; very offensive odour; B.P. 78°. (J. pr., [1], 30, 319.)

**Reaction CXXXV. Action of Chloroform and Alcoholic Potash on Aliphatic and Aromatic Primary Amines.**

$$R.NH_2 + CHCl_3 + 3KOH \rightarrow R.NC + 3KCl + 3H_2O.$$

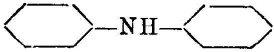
The isonitriles formed have a characteristic poisonous odour. When used as a test for primary amines they should be destroyed (hydrolysed) by pouring into conc. hydrochloric acid—using a fume cupboard for the entire operation.

**Reaction CXXXVI. Action of the Hydrochloride of a Primary Aromatic Base on the Base.**

$$R.NH_2 + HCl.NH_2R \rightarrow R.NH.R + NH_4Cl.$$

The reaction takes place at a high temperature and usually under high pressure in an autoclave, secondary amines being formed.

PREPARATION 264.—**Diphenylamine.**

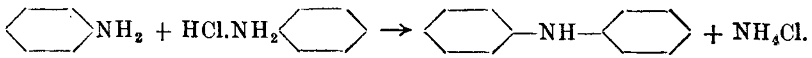


$C_{12}H_{11}N.$ 169.

93 gms. aniline and 93 gms. aniline hydrochloride are heated for 20 hours at 230° in an enamelled autoclave, the pressure reaching about 6 atms. Iron should not be in contact with the reaction products; it reduces the yield. After 2 hours, the water present is cautiously blown off through the valve, this process being repeated three times during an hour. The presence of water has a very marked influence on the reaction. Some aniline and ammonia also escape. The reaction is complete after about 20 hours. The contents of the autoclave are then placed in a porcelain basin with a litre of water, and heated to 80°. 70 c.cs. strong hydro-

chloric acid are added until the reaction is just acid to Congo Red. It is then allowed to cool. After several hours the crude diphenylamine separates as a solid cake, which can easily be removed from the mother liquor. It is then melted under a little water, and any unchanged aniline extracted with a little hydrochloric acid, and washed with dilute sodium carbonate. The diphenylamine is then purified by distillation with superheated steam (see p. 25), the temperature of the oil bath being 250°, and that of the superheated steam 300°. The diphenylamine is obtained as an almost colourless liquid, which solidifies to a pale yellow cake.

Aniline can be recovered from the acid mother liquors.



*Yield.*—60% theoretical (100 gms.). Colourless crystals; peculiar smell; M.P. 53°; B.P. 310°; important intermediate for dyestuffs. (B., 40, 4541.)

**Reaction CXXXVII. Action of Bromine (or Chlorine) and Alkali on certain Amides and Imides** (Hoffmann's Reaction).—This method is applicable for the preparation of both aliphatic and aromatic amines.

$$R.CO.NH_2 + Br_2 \rightarrow R.CO.NHBr + HBr.$$
$$R.CO.NHBr \rightarrow R.N:CO + HBr.$$
$$RNCO + H_2O \rightarrow R.NH_2 + CO_2.$$

The reaction proceeds in stages, a bromamide being first formed; this loses a molecule of hydrogen bromide on further action with caustic soda, yielding probably an isocyanate, which, being unstable in presence of excess of alkali, is hydrolysed to an amine and carbon dioxide. Sodium hypochlorite (or hypobromite) and sodium hydroxide are the reagents used. The reaction finds industrial application in the preparation of anthranilic acid for the synthesis of indigo. On a technical scale sodium hypochlorite is always employed, but on a small scale sodium (or potassium) hypobromite is frequently used owing to the ease with which a solution of known strength can be made up from weighed quantities of bromine and alkali. (See also Reaction CLXIV.)

Preparation 265.—**Anthranilic Acid** (*o-Aminobenzoic acid*).

$$C_6H_4\left\langle\begin{array}{l}NH_2\\COOH\end{array}\right. \qquad C_7H_7O_2N. \qquad 137.$$

40 gms. of finely powdered phthalimide and 80 gms. of caustic soda are dissolved together in 280 c.cs. of water, the solution being cooled during the operation. The solution is agitated, and 400 gms. of a 5% solution of sodium hypochlorite run in. When all is added, the solution is warmed for a few minutes at 80° to complete the reaction; it is then cooled and neutralised exactly with hydrochloric or sulphuric acid. An excess of strong acetic acid is added to precipitate the anthranilic acid,

which is filtered off and washed with water. Any anthranilic acid remaining in the filtrate is precipitated as copper anthranilate by the addition of a saturated solution of copper acetate. After standing for some time the precipitate is filtered off and suspended in a small quantity of warm water, while a current of sulphuretted hydrogen is passed into the suspension. The copper sulphide formed is filtered off, and anthranilic acid recovered from the filtrate by concentration on a water bath. It may be recrystallised from hot water.

$$C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle NH \rightarrow C_6H_4\left\langle\begin{matrix}NH_2\\COOH.\end{matrix}\right.$$

*Total Yield.*—85% theoretical (31·5 gms.). M.P. 145°. (D.R.P., 55988; J. Soc. Dyers, 1901, 17, 139.)

**Reaction CXXXVIII. Action of Heat on Ammonium Salts.**—Ammonium salts of monobasic acids yield amides.

$$R.COONH_4 \rightarrow R.CO.NH_2 + H_2O.$$

While those of dibasic acids yield imides.

$$\begin{matrix}CH_2COOH\\|\\CH_2.COONH_4\end{matrix} \rightarrow \left.\begin{matrix}CH_2.CO\\|\\CH_2.CO\end{matrix}\right\rangle NH + 2H_2O.$$

Preparation 266.—**Acetamide.**

$$CH_3CO.NH_2. \quad C_2H_5ON. \quad 59.$$

20 gms. ammonium acetate (as dry as possible), and 25 gms. glacial acetic acid are placed in a small round-bottomed flask provided with a reflux condenser, and heated to gentle boiling over a wire gauze for 3 hours. The flask is then connected by means of a cork and delivery tube with a sloping water condenser, and distillation commenced. The distillate up to 160° is discarded. Above 160° the water is run out of the condenser and the distillate collected in a small distilling flask. This portion is redistilled and the fraction 210°—225° separately collected; it solidifies on cooling to a mass of white crystals. These may be recrystallised from ether as long needles.

$$CH_3.COONH_4 \rightarrow CH_3.CONH_2 + H_2O.$$

*Yield.*—80% theoretical (12 gms.). M.P. 82°; B.P. 222°. (B., 15, 980.) For modification of above, see Am. Soc., 44, 2286, and O. S., IX., 90.

Preparation 267.—**Succinimide** [*Imide of butan-diacid*].

$$\left.\begin{matrix}CH_2.CO\\|\\CH_2.CO\end{matrix}\right\rangle NH. \quad C_4H_5O_2N. \quad 99.$$

20 gms. of succinic acid are dissolved in a small quantity of water in a basin, and the solution neutralised with ammonia. The solution is boiled to expel excess of ammonia, after which a further 20 gms. of succinic acid dissolved in water are added. The solution is evaporated to complete dryness on a water bath; the dry residue is transferred to a

retort and heated quickly with a large luminous flame. The sublimate of succinimide is recrystallised from pure acetone.

$$\begin{array}{l} CH_2.COOH \\ | \\ CH_2.CO.ONH_4 \end{array} \rightarrow \begin{array}{l} CH_2.CO \\ | \\ CH_2.CO \end{array}\!\!\!>NH + 2H_2O.$$

*Yield.*—70% theoretical (11 gms.). Colourless rhombic plates; M.P. 126°; B.P. 288°. (A., 49, 198.)

PREPARATION 268.—**Formamide.**

$H.CONH_2$. $CH_3ON$. 45.

150 c.cs. of pure formic acid are placed in a round-bottomed flask attached to a condenser, and having also a delivery tube dipping nearly to the bottom of the acid in the flask. Dry ammonia gas is led into the acid through the delivery tube, passing first through a tower of solid caustic soda, and then soda-lime. Much heat is evolved during the reaction, and the flask must be cooled. After about 15 minutes the acid is neutralised, and crystals of ammonium formate are deposited. The flask is then heated on a paraffin bath, and at 150° the salt begins to decompose and water passes over. The temperature is gradually raised to 180°, at which temperature no more water distils over. The resulting brown liquid is distilled under greatly reduced pressure, the fraction 85°—95° at 0·5 mm. being collected. After standing over anhydrous sodium sulphate for some days, it is again distilled under reduced pressure.

$$H.COONH_4—H_2O \rightarrow H.CONH_2.$$

*Yield.*—66% theoretical (98 gms.). Viscous colourless liquid; M.P. 2·25°; $D.^{14}$ 1·337. (Am. Soc., 40, 794.)

**Reaction CXXXIX. Action of Ammonia on Esters, Acid Chlorides or Anhydrides.**

(1) $$R.COOR_1 + NH_3 \rightarrow R.CO.NH_2 + R_1OH.$$

(2) $$R.COCl + NH_3 \rightarrow R.CO.NH_2 + HCl.$$

(3) $$\begin{array}{l} RCO \\ RCO \end{array}\!\!>O + 2NH_3 \rightarrow 2R.CO.NH_2 + H_2O.$$

(1) Is restricted mostly to esters of aliphatic acids. (2) Is employed for the preparation of aromatic amides. If the anhydride of a dibasic acid, *e.g.*, phthalic, is employed, an imide results.

PREPARATION 269.—**Acetamide.**

15 gms. ethyl acetate are treated in a small flask with an equal weight of conc. ammonia solution. The flask is loosely corked and left in a warm place (say, near a steam bath) until the two layers originally present give place to one uniform solution. This solution is then distilled, water, alcohol and ammonia passing over up to 100°; the fraction 210°—225° is separately collected, and if it does not solidify on cooling it is redistilled. The final product is recrystallised from ether.

$$CH_3.CO.OC_2H_5 + NH_3 \rightarrow CH_3.CONH_2 + C_2H_5.OH.$$

*Yield.*—80% theoretical (8·5 gms.). M.P. 82°. (B., 15, 981; Am. Soc., 33, 974.)

Oxamide is obtained as a white amorphous precipitate when equal weights of dimethyl (or diethyl) oxalate and conc. ammonia are mixed. The precipitate is filtered off and recrystallised from alcohol.

$$CH_3O.OC.CO.OCH_3 + 2NH_3 \rightarrow NH_2OC.CONH_3 + 2CH_3OH.$$

PREPARATION 270.—**Benzamide.**

$$C_6H_5.CONH_2. \qquad C_7H_7ON. \qquad 121.$$

10 gms. finely powdered dry ammonium bicarbonate are placed in a mortar in a fume cupboard. 5 gms. benzoyl chloride are added and the whole well mixed with a pestle during 10 minutes. If the odour of benzoyl chloride persists at the end of this time, a few drops of conc. ammonia are added. The product is diluted with water, the benzamide filtered off and recrystallised from boiling water.

$$C_6H_5COCl + 2NH_4HCO_3 \rightarrow C_6H_5CONH_2 + NH_4Cl + 2CO_2 + 2H_2O.$$

*Yield.*—93% theoretical (4 gms.). Glistening plates; M.P. 130°. (A., 3, 268; B., 10, 1785; J. C. S., 1930, 2788.)

Benzamide may also be prepared by adding 5 gms. benzoyl chloride drop by drop to 20 c.cs. conc. ammonia solution.

PREPARATION 271.—**Phthalimide.**

$$C_6H_4{<}^{CO}_{CO}{>}NH. \qquad C_6H_5O_2N. \qquad 147.$$

20 gms. phthalic anhydride are placed in a 100-c.c. conical flask fitted with a cork carrying inlet and exit delivery tubes. The flask is heated in a paraffin-wax bath until the anhydride melts, when a current of dry ammonia is led in through the inlet tube, which reaches to within 1 cm. of the substance. The temperature of the bath is gradually raised during an hour to 230°. The contents of the flask are then cooled and recrystallised from ether.

$$C_6H_4{<}^{CO}_{CO}{>}O + NH_3 \rightarrow C_6H_4{<}^{CO}_{CO}{>}NH + H_2O.$$

*Yield.*—90% theoretical (14 gms.). White needles; M.P. 232°. (A., 247, 294; B., 10, 579; O. S., II., 75.)

**Reaction CXL. Action of Ammonia on Phenols and Sulphonic Acids.**

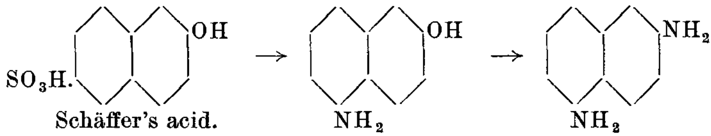
$$(1) \qquad R.OH + NH_3 \rightarrow R.NH_2 + H_2O.$$
$$(2) \qquad R.SO_3H + NH_3 \rightarrow R.NH_2 + H_2SO_3.$$

(1) Takes place readily with polyhydric phenols and naphthols, also if negative groups are present in the molecule, *e.g.*, nitrophenols (B., 19, 2161.)

The reaction is usually carried out under pressure, and the yield is improved by the presence of sodium or ammonium sulphite (Bucherer's method), the sulphurous esters of phenols reacting more readily than

phenols. Concentrated ammonia is used, or the addition compound with zinc chloride. Reaction (2) is carried out similarly to (1) and takes place readily in the anthraquinone series, but not in the naphthalene series, where sodamide is sometimes used. (B., 1906, 3009.) For use of barium amide, see Am. Soc., 1934, 1748.

An interesting case of group migration may be mentioned here.



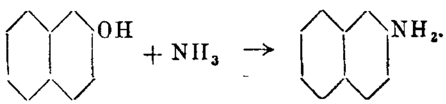
Schäffer's acid.

For preparation of primary, etc., amines from alcohol, see E. P., 410500.

PREPARATION 272.—$\beta$-**Naphthylamine** (2-*Aminonaphthalene*).

$C_{10}H_9N$. 143.

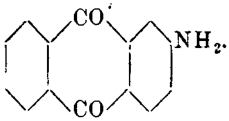
*Method I.*—144 gms. $\beta$-naphthol and 600 gms. ammonium sulphite are placed in an autoclave with stirrer and oil bath. 125 gms. 20% ammonia are also added, and the mixture is heated for 8 hours at an internal temperature of 150°, and a pressure of 6 atms. (*Note.*—Brass gauges should not be used.) The contents are allowed to cool and the cake of $\beta$-naphthylamine is broken up and thoroughly washed with water on a filter. After washing it is dissolved in 1½ litres of water and 110 gms. hydrochloric acid (which should be free from sulphuric acid) and filtered. To the filtrate are added about 400 gms. saturated sodium sulphate solution until precipitation of the naphthylamine sulphate is complete (test). It is then filtered and washed with water. The free base is obtained by making a thin paste of the sulphate and heating to 80° with stirring, when caustic soda solution is added until the liquid gives an alkaline reaction to phenolphthalein. It is then filtered, washed and dried at 80°.




*Yield.*—85—95% theoretical (120—135 gms.). White plates; M.P. 112°; B.P. 294°; the sulphate is less soluble than that of $\alpha$-naphthylamine; important intermediate for dyestuffs. (E.P., 1387, 1900; F.P., 297464, 394820.)

*Method II.*—50 gms. $\beta$-naphthol and 200 gms. powdered zinc-ammonium chloride are mixed and heated on an oil bath in a vessel provided with a reflux condenser for 2 hours at 200°. The product, after cooling, is treated with 25% caustic soda solution until the zinc oxide redissolves, and the solution boiled for a few minutes. On cooling, $\beta$-naphthylamine separates. It may be removed and purified, as described in Method I. It may also be separated by extraction with ether, or by distillation in a current of superheated steam. (B., 13, 1300.)

PREPARATION 273.—**2-Aminoanthraquinone.**



$C_{14}H_9O_2N$. 223.

20 gms. sodium anthraquinone sulphonate ("silver salt") and 200 c.cs. of conc. aqueous ammonia (D. 0·88) are heated in an autoclave of 500 c.cs. capacity to 180°, and maintained at this temperature for 6 hours. The autoclave is left to cool overnight, then opened, and the aminoanthraquinone filtered off and dried.

Red crystals; M.P. 302°. (B., 12, 1567; E.P., 358852.)

**Reaction CXLI. Action of Acids, Acid Anhydrides and Chlorides on Primary and Secondary Amines.**—Substituted amides are usually prepared by treating amines with organic acids, or with acyl chlorides or anhydrides. When the acid is used a salt is first formed from which a molecule of water is eliminated on further heating.

$$RCOOH + R_1NH_2 \rightarrow R.COONH_3R_1 \rightarrow R.CONHR_1 + H_2O.$$
$$RCOCl + R_1NH_2 \rightarrow R.CONHR_1 + HCl.$$
$$(RCO)_2O + 2R_1NH_2 \rightarrow 2RCONHR_1 + H_2O.$$

When benzoyl chloride is used it is necessary to have present, or to add subsequently, an excess of caustic soda or some other basic substance (Schotten-Baumann Reaction).

When an acid anhydride is used the reaction is usually carried out by the application of heat, and may be hastened by the addition of dehydrating agents, *e.g.*, fused sodium acetate or fused zinc chloride.

PREPARATION 274.—**Acetanilide** [*Phenyl-amide of ethan acid*].

$CH_3CONHC_6H_5$. $C_8H_9ON$. 135.

A mixture of 25 gms. (1 mol.) of redistilled aniline and 30 gms. (excess) of glacial acetic acid is boiled under an air condenser, preferably in a flask with a condenser ground into the neck, until no aniline separates on treating a sample with a cold caustic soda solution (8 hours). The hot liquid is at once poured into 500 c.cs. of cold water, filtered, and washed with cold water. The crude acetanilide is boiled with a litre of water, a little alcohol being added until it all goes into solution. It is filtered through a hot water filter (see p. 11), and the solution allowed to crystallise. If the product is dark coloured, it is redissolved as before, boiled with 5 gms. of animal charcoal for $\frac{1}{2}$ hour, filtered, and allowed to crystallise.

*Yield.*—85% theoretical (30 gms.). Rhombic plates; sparingly soluble in hot water; M.P. 112°; B.P. 295°. (J. C. S., 2, 106.)

If 10 gms. of fused sodium acetate (see p. 503) are added to the reaction mixture, the time of heating can be shortened to 6 hours. An older method of working up the reaction product was to distil fractionally the mixture of acetanilide and excess acetic acid, the former coming over at 280°, and being then recrystallised (A. Ch., [3], 37, 328).

PREPARATION 275.—**Benzanilide** (*Phenylamide of benzenecarboxylic acid*).

$C_6H_5NH.CO.C_6H_5$. $C_{13}H_{11}ON$. 97.

*Method I.*—12 gms. of aniline are placed in a dish in a fume cupboard, and 10 gms. of benzoyl chloride are gradually added. Much heat is developed. When cold the product is extracted first with dilute hydrochloric acid to remove aniline, then with dilute caustic soda to remove benzoic acid, and finally with water. After pressing it is crystallised from alcohol.

$$C_6H_5.CO.Cl + 2C_6H_5NH_2 \longrightarrow C_6H_5.CO.NH.C_6H_5 + C_6H_5NH_2.HCl.$$

*Yield.*—Almost theoretical (20 gms.). (A., 60, 311.)

In the above process only one-half of the amine is transformed into its benzoyl derivative. By working in presence of dilute caustic soda or other alkali (Schotten-Baumann Reaction, see benzoyl-*p*-toluidine), the amine is completely converted into its benzoyl derivative.

*Method II.*—A mixture of 15 gms. (1 mol.) of aniline, and 20 gms. (1 mol.) of benzoic acid is heated in a retort at 180°, and the temperature raised gradually to 225°; a further 10 gms. of aniline are added, and heating continued. The hot mass is then poured into an evaporating dish and allowed to solidify. It is powdered, washed with dilute hydrochloric acid to remove unchanged base, then with water to remove the benzoate, then with dilute caustic soda to remove free acid, and finally with water. It is dried and crystallised from alcohol.

$$\begin{gathered} C_6H_5NH_2 + C_6H_5COOH \longrightarrow C_6H_5NH_2.C_6H_5COOH \\ \longrightarrow C_6H_5NHCOC_6H_5 + H_2O. \end{gathered}$$

*Yield.*—80% theoretical (26 gms.). Colourless plates; insoluble in water; M.P. 162°. (Bl., [3], 11, 8933; O. S., VII., 6.)

PREPARATION 276.—**Benzoyl-*p*-toluidide** (p-*Toluoyl-amide of benzene carboxylic acid*).

$$C_6H_5CONH.C_6H_4CH_3[1:4]. \qquad C_{14}H_{13}ON. \qquad 211.$$

2 gms. (1 mol.) of finely divided *p*-toluidine are mixed with 10 c.cs. of a 10% aqueous solution of sodium hydroxide, and 2 c.cs. benzoyl chloride (excess) are added gradually to the warm mixture in a corked flask, which is mechanically shaken. Thorough shaking is essential. If any excess of benzoyl chloride remains, it is destroyed by warming with a further quantity of sodium hydroxide solution. The mixture is then poured into water, and the precipitate filtered, dried, and recrystallised from alcohol.

$$CH_3C_6H_4NH_2 + C_6H_5COCl + NaOH = C_6H_5CONHC_6H_4CH_3 + NaCl + H_2O.$$

*Yield.*—Almost theoretical (4 gms.). Colourless crystals; insoluble in water; M.P. 158°. (B., 19, 3219.)

PREPARATION 277.—**Diaceto-*o*-toluidide.**

$$CH_3.C_6H_4N(CO.CH_3)_2[1:2]. \qquad C_{11}H_{13}O_2N. \qquad 191.$$

10 gms. of *o*-toluidine, 38 gms. of acetic anhydride and 5 gms. fused sodium acetate are heated to boiling for 1 hour in a flask provided with an air condenser and calcium chloride tube. After this time the product is distilled from a distilling flask at a pressure of 20 mms. Acetic acid and

acetic anhydride pass over first; then diacetyl derivative distils at 152°—153°, and sodium acetate and some mono-acetyl derivative remain in the flask.

$$CH_3.C_6H_4NH_2 + (CH_3CO)_2O \rightarrow CH_3.C_6H_4N(COCH_3)_2 + H_2O.$$

*Yield.*—80% theoretical (14 gms.). Colourless crystals; somewhat unstable; M.P. 18°. (B., 26, 2855.)

**Reaction CXLII. Action of Primary Aromatic Amines on Alcohols.**—The reaction is generally carried out by heating under pressure, and in presence of a mineral acid. Secondary and tertiary amines are formed.

$$RNH_2 + R_1OH \rightarrow RNHR_1 + H_2O.$$
$$R.NHR_1 + R_1OH \rightarrow RN(R_1)_2 + H_2O.$$

PREPARATION 278.—**Dimethylaniline.**

$$C_6H_5N(CH_3)_2. \qquad C_8H_{11}N. \qquad 121.$$

93 gms. pure aniline, 105 gms. pure methyl alcohol and 9·4 gms. conc. sulphuric acid are heated in an enamelled autoclave to 200°. The pressure rises to about 30 atms., and the contents are left for 6 hours at 215°. They are allowed to cool, and then 25 gms. 30% caustic soda solution added. The product is now heated to 170° in the autoclave for a further 5 hours. This second heating is necessary to decompose the sulpho-ammonium bases formed, and which are decomposed into sulphuric acid, alcohol, and tertiary amine. The contents of the autoclave, after cooling, are distilled in steam. The dimethylaniline is salted out of the distillate with common salt. It is then separated and distilled.

$$C_6H_5N\begin{array}{|ccc|}H_2 & + & HO \\ & & HO\end{array}\begin{array}{l}CH_3 \\ CH_3\end{array} \rightarrow C_6H_5N.(CH_3)_2.$$

*Yield.*—95% theoretical (117 gms.). Colourless liquid when pure; turns brown on standing; B.P. 192°; D. 0·96; important intermediate for dyestuffs.

*Purity Test* (anhydride test).—Some monomethylaniline is always present, and if 4 c.cs. of the dimethylaniline are shaken up with 2 c.cs. acetic anhydride, this should not give an increase in the temperature of more than 1° (C. Z., 34, 641).

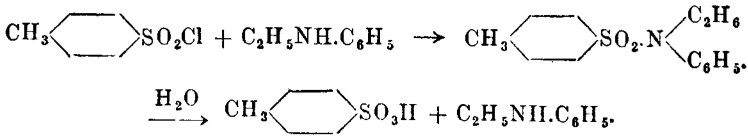
PREPARATION 279.—**Diethylaniline.**

$$C_6H_5N(C_2H_5)_2. \qquad C_{10}H_{15}N. \qquad 149.$$

130 gms. dried aniline hydrochloride and 140 gms. 95% alcohol are heated in an enamelled autoclave at 180° for 8 hours. After cooling, the contents of the autoclave are placed in a round-bottomed flask and the alcohol and ethyl ether distilled off. The residual mixture of mono- and diethylaniline is treated with 110 gms. 30% caustic soda solution. The product is stirred up at ordinary temperature with 40 gms. of *p*-toluene sulphonic chloride, which forms a non-volatile derivative with the monoethylaniline. The diethylaniline is then distilled from the mixture in steam, and separated as in Preparation 278.

The monoethylaniline can be obtained by hydrolysing the toluene sulphonic derivative with conc. sulphuric acid.

$$C_6H_5NH_2 + \begin{matrix} HOC_2H_5 \\ HOC_2H_5 \end{matrix} \rightarrow C_6H_5N(C_2H_5)_2.$$



*Yield.*—80% theoretical (120 gms.). Colourless liquid when pure; B.P. 216·5°; D. 0·939; important intermediate for dyestuffs. (A., 74, 128; D.R.P., 250236.)

**Reaction CXLIII. Condensation of Aromatic Aldehydes with Primary Aromatic Amines.**—Anil formation takes place readily on heating.

$$R.CHO + NH_2R_1 \rightarrow RCH = NR_1 + H_2O.$$

Substituted aldehydes and substituted amines also react: for example, the sodium salt of α-naphthylamine 4-sulphonic acid when dissolved in water and shaken with an alcoholic solution of benzaldehyde yields sodium benzylidine naphthionate.

With aliphatic aldehydes the reaction takes the following course:—

$$CH_3.CHO + 2NH_2.C_6H_5 \rightarrow CH_3CH(NH.C_6H_5)_2 + H_2O.$$

Formaldehyde reacts like the aromatic aldehydes, yielding dehydroformaldehyde (or methylene) compounds.

$$C_6H_5NH_2 + OCH_2 \rightarrow C_6H_5N = CH_2 + H_2O.$$

PREPARATION 280.—**Benzylideneaniline.**

$$C_6H_5N = CH.C_6H_5. \qquad C_{13}H_{11}N. \qquad 181.$$

9·3 gms. of aniline (1 mol.) and 10·6 gms. of benzaldehyde (1 mol.) are placed in a porcelain dish on an oil bath and heated for 5 hours at 125°. The product, while still warm, is poured into ice-water with stirring. Benzylideneaniline solidifies, is filtered and washed. The product can be used directly for the preparation of *p*-nitroaniline. It is insoluble in water, but can be recrystallised from alcohol.

$$C_6H_5NH_2 + OCH.C_6H_5 \rightarrow C_6H_5N = CH.C_6H_5 + H_2O.$$

*Yield.*—85% theoretical (15 gms.). M.P. 54°. (J., 1850, 488; O. S., VIII., 22.)

**Reaction CXLIV. Action of Ammonia on Aldehydes.**—The simplest case is the formation of an aldehyde ammonia by the action of dry ammonia gas on the aldehyde in dry ethereal solution. Acetaldehyde and several of the aliphatic aldehydes react after this fashion. (See Preparation 440.)

$$R.CHO + NH_3 \rightarrow R.CHOH.NH_2.$$

Formaldehyde and most of the aromatic aldehydes do not react in this way with ammonia, but form complex condensation products. (See below.) Glucose and other monosaccharides condense with ammonia and amines to give glucamines; *e.g.*, hydrogen and ethylamine at 90°–100° and 100 atms. in presence of nickel-kieselgühr (p. 172) give ethylglucamines, $C_2H_5NH.CH_2.(CHOH)_4CH_2OH$. (E.P., 426062.)

PREPARATION 281.—**Hexamethylenetetramine** (*Hexamine*).

$(CH_2)_6N_4$. $C_6H_{12}N_4$. 140

50 c.cs. of "formalin" containing 40% formaldehyde and 30 c.cs. of conc. ammonium hydroxide solution (D. 0·88) are mixed in a round-bottomed flask. The flask is connected to a suction pump and the contents evaporated on a water bath under diminished pressure to a thick paste. A second equal quantity of ammonium hydroxide is then added and evaporated, as before. The residue is treated with sufficient boiling absolute alcohol to dissolve, filtered hot, and the filtrate set aside to cool. Colourless crystals separate, which are filtered off and washed with a little absolute alcohol.

$$6CH_2O + 4NH_4OH \rightarrow (CH_2)_6N_4 + 10H_2O.$$

*Yield.*—80% theoretical (12·5 gms.). Sublimes about 260°; very soluble in water. (B., 19, 1842.)

PREPARATION 282.—**Hydrobenzamide.**

$(C_6H_5CH)_3N_2$. $C_{21}H_{18}N_2$. 298.

5 c.cs. of benzaldehyde and 25 c.cs. conc. ammonium hydroxide solution are placed in a stoppered flask and allowed to stand for 2 days. Crystals of hydrobenzamide separate, which are filtered off, washed with water, and recrystallised from alcohol.

$$3C_6H_5CHO + 2NH_3 = C_6H_5CH\left\langle\begin{matrix}N : CH.C_6H_5\\N : CH.C_6H_5\end{matrix}\right. + 3H_2O.$$

*Yield.*—90% theoretical (4·2 gms.). M.P. 110°; insoluble in water, easily soluble in alcohol. (A., 21, 130.)

**Reaction CXLV. Action of Nitrous Acid on certain Ketones.**—Iso-nitroso compounds are formed by the action of nitrous acid on ketones which contain the **$CH_2$.CO**—group.

$$\text{—}CH_2.CO\text{—} + HONO \rightarrow \begin{matrix}\text{—}C.CO\text{—}\\ \| \\ NOH\end{matrix} + H_2O.$$

PREPARATION 283.—*iso***Nitrosocamphor.**

$$C_8H_{14}\left\langle\begin{matrix}C : NOH\\ | \\ CO.\end{matrix}\right. \qquad C_{10}H_{15}O_2N. \qquad 181.$$

102 gms. of camphor are dissolved in 550 c.cs. of pure dry ether in a litre flask, and 15·2 gms. sodium wire added. The flask is well cooled in a mixture of ice and salt, and 78 gms. of isoamylnitrite added in small portions, the flask being thoroughly shaken after each addition. After standing for an hour, during which time a part of the sodium iso-nitroso camphor separates, the contents of the flask are slowly poured into ice-water. An ethereal layer, containing borneol and unchanged camphor, separates, while the reddish-yellow aqueous layer contains the sodium iso-nitroso camphor. The aqueous layer is separated, extracted twice with ether, and any dissolved ether removed from it by blowing a current

of air through it. It is then neutralised with dilute acetic acid when the iso-nitroso camphor is precipitated. The precipitate is filtered off, washed with water, and after being dried in a steam bath is recrystallised from a mixture of petroleum ether and benzene.

$$C_8H_{14}\left<\begin{array}{l}CH_2\\ |\\ CO\end{array}\right. + C_5H_{11}ONO \longrightarrow C_8H_{14}\left<\begin{array}{l}C:NOH\\ |\\ CO\end{array}\right. + C_5H_{11}OH.$$

*Yield.*—30% theoretical (35 gms.). Long prisms; M.P. 152°—154°; easily soluble in ether, alcohol, alkali and benzene; difficultly soluble in petroleum ether. (A., 274, 73.)

# CHAPTER XX

## THE LINKING OF SULPHUR TO CARBON

### Sulphonic Acids

**Reaction CXLVI. Action of Concentrated Sulphuric Acid on Hydrocarbons or Substituted Hydrocarbons.**—When conc. sulphuric acid acts on an aromatic hydrocarbon or substituted hydrocarbon, one or more of the H atoms in the nucleus is replaced by the sulphonic group ($SO_2.OH$).

$$R.H + H_2SO_4 \longrightarrow R.SO_2OH + H_2O.$$

It is necessary to use a large excess of conc. $H_2SO_4$. In this way the concentration of the acid is little affected by the amount of water formed in the reaction. Indeed, when the sulphuric acid reaches a minimum concentration (78% in the case of benzene) sulphonation does not go to completion.

Some sulphonic acids, *e.g.*, benzene and toluene sulphonic acids, may be formed at ordinary temperatures, while others require a considerably higher temperature. In some cases 100% $H_2SO_4$ (monohydrate—$SO_3.H_2O$) is necessary. The influence of temperature (see table below), concentration of acid, time of reaction, and the presence of other substituents is very marked, and different isomers are formed under different conditions.

Effect of Temperature on Sulphonation of Toluene :

| Temp. | *ortho* | *meta* | *para* |
|---|---|---|---|
| 0° | 42·7 | 3·8 | 53·5% |
| 35° | 31·9 | 6·1 | 62·0% |
| 100° | 13·3 | 8·0 | 78·7% |

The reaction may be assisted mechanically by mixing with kieselgühr, or other finely divided material, and catalytically by the addition of iodine, or alkali metavanadate (U.S.P., 1915925) in the case of benzene, and of boric acid, mercury and mercury salts in the case of anthraquinone.

The sulphonic group is strongly acidic, and will decompose carbonates with the formation of stable salts, a property which is used in their separation. The presence of a basic group in the nucleus is not sufficient to neutralise its acidity, thus sulphanilic acid is distinctly acid.

**Isolation of Sulphonic Acids.**—Sulphonic acids are usually isolated in the form of their salts in order to get rid of the excess of sulphuric acid used in the reaction. The calcium or barium salts are formed where these are soluble by adding lime or barium carbonate, and the excess sulphuric acid precipitated as $CaSO_4$ or $BaSO_4$, and removed by filtra-

tion. The filtrate containing the salt in solution may then be concentrated till the salt crystallises out or it may be evaporated to dryness. The sodium salt may be obtained from the sulphonation mixture by diluting and adding a saturated solution of common salt, and allowing to crystallise. Isomers may be separated by the fractional crystallisation of their salts; it is often best, however, to form the sulphonyl chlorides by treatment with $PCl_5$, and then the sulphonamides by the action of ammonia (see Prep. 291); after fractional crystallisation of the amides the acids are set free by heating under pressure with hydrochloric acid. The sulphonyl chlorides, and the sulphonamides which generally crystallise well and have definite melting points, are used for the identification of sulphonic acids.

**Tests for Complete Sulphonation.**—The sulphonation is tested by the solubility of the product in water or dilute alkali. Complete solubility is seldom obtained owing to the formation of a sulphone by condensation.

$$R.SO_3H + H.R \longrightarrow R.SO_2.R + H_2O.$$

The sulphones are insoluble in water, but may be distinguished, say, from unchanged naphthalene by extracting and taking the melting point. The following factors influence the formation of sulphones; concentration of acid ($H_2SO_4$ or $SO_3$), temperature of sulphonation, duration of sulphonation. Conditions have to be chosen so that the quantity of sulphone is reduced to a minimum.

**Apparatus used in Sulphonation.**—The most convenient type of apparatus for this process is a cast-iron pot with a good mechanical agitator, a thermometer pocket, and an opening for reflux condenser (see Fig. 37). It is of the utmost importance that the agitation should be as efficient as possible. Fig. 38 shows a convenient apparatus in glass, when the cast-iron pot is not procurable.

PREPARATION 284.—**Benzenesulphonic Acid.**

$$C_6H_5.SO_3H. \qquad C_6H_6O_3S. \qquad 158.$$

*Method I.*—300 gms. of conc. sulphuric acid (96%) and 60 gms. of benzene are placed in the sulphonating vessel and the temperature raised to the boiling point of benzene, 80°, the agitation being maintained from the commencement of the heating. The benzene vapour is condensed and returned by the reflux. The heating is continued for 8—10 hours, when the sulphonation should be complete (test). Milk of lime is made up in a basin by adding 1 part of lime to 5 parts of hot water, and stirring. The sulphonation is cooled and poured into 300 c.cs. of water.

*Isolation of Calcium Salt.*—The milk of lime is now carefully added with stirring until the solution is just neutral (test with phenolphthalein paper). It is then boiled, and after cooling to 60° the $CaSO_4$ is filtered off on a Buchner funnel, and washed with a little hot water.

*Isolation of Free Acid.*—To the filtrate which contains the Ca salt in solution, dilute sulphuric acid is added until all the Ca is precipitated (test), and this is filtered off and washed with a little hot water. The filtrate is then evaporated until the free acid crystallises out.

*Isolation of Sodium Salt.*—The sodium salt is isolated when fusion with caustic soda is anticipated. To the filtrate containing the Ca salt in solution, sodium carbonate is added until no more $CaCO_3$ is precipitated (test). The $CaCO_3$ is filtered off and washed, and the filtrate evaporated, yielding the Na salt.

If the sulphonation mixture is treated with lime so as to give a neutral reaction to litmus, the completion of the formation of the sodium salt can then be conveniently judged when an alkaline reaction to phenolphthalein is obtained during the addition of sodium carbonate.

$$C_6H_6 + H_2SO_4 \rightarrow C_6H_5.SO_3H + H_2O.$$

*Yield.*—75—80% theoretical. Na and Ca salts, white powders, soluble in water; used in preparation of phenol, see p. 210.

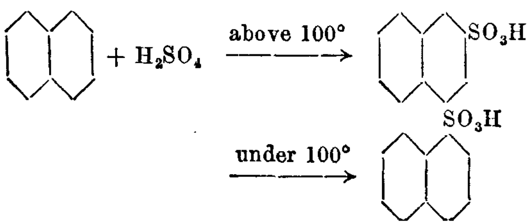
*Method II.*—15 gms. pure benzene, 90 gms. of sulphuric acid (D. 1·842) and sufficient washed and ignited kieselgühr to form a thin paste are shaken together and allowed to stand for 24 hours. The acid is isolated as before.

*Yield.*—Theoretical (30 gms.). (D.R.P., 71556.)

PREPARATION 285.—**Naphthalene-$\beta$-sulphonic Acid (Na salt).**

$$C_{10}H_7SO_3H. \qquad C_{10}H_8SO_3. \qquad 208.$$

120 gms. of conc. sulphuric acid are heated to 160° and 100 gms. of melted naphthalene poured in from a basin, good agitation being maintained. When all the naphthalene is added, the temperature is raised to 170° for 3 hours, and then to 180° for 1 hour, until sulphonation is complete (test). Excess sulphuric acid is removed as $CaSO_4$, as in benzene sulphonic acid. The filtrate containing the calcium salt of the $\beta$-acid as well as some calcium salt of the $\alpha$-acid is concentrated until a sample, on cooling, sets to a thick mass. It is allowed to crystallise overnight, and filtered. The sodium salt is isolated as above.




$\beta$-acid.

$\alpha$-acid.

*Yield.*—75% theoretical (130 gms.). White powder; soluble in water; used in preparation of $\beta$-naphthol. (Rec., 36, 20, 197.)

For the conversion of $\alpha$- into $\beta$-derivatives, see B., 67, 67.

PREPARATION 286.—***d*-Camphorsulphonic Acid** (*Reychler's Acid*).

$$C_{10}H_{15}O.SO_3H. \qquad C_{10}H_{16}O_4S. \qquad 232.$$

45 gms. (1 mol.) of camphor are finely powdered and added to a well-stirred mixture containing 30 gms. (1 mol.) of conc. sulphuric acid, and 60 gms. of acetic anhydride. The camphor dissolves readily, and the solution is allowed to stand for 2—3 days until no more *d*-camphor sulphonic acid crystallises out. The crystals are then filtered through

asbestos or glass wool, washed with acetic acid until colourless, and recrystallised from acetic acid or ethyl acetate.

$$C_{10}H_{16}O + H_2SO_4 \rightarrow C_{10}H_{15}O.SO_2OH + H_2O.$$

*Yield.*—50% theoretical (35 gms.). Large prisms; decompose at 193°; $[a]_D = +21°$. (Bl., [iii], 19, 120; J. C. S., 81, 1442.)

PREPARATION 287.—*o*- **and** *p*-**Toluenesulphonic Acids.**

$$C_6H_4\begin{cases} CH_3 \\ SO_3H. \end{cases} \qquad C_7H_8O_3S. \qquad 172.$$

130 gms. pure toluene are heated with 450 gms. conc. sulphuric acid in a cast-iron pot fitted with a suitable agitator (see Fig. 37). A crystal of iodine is added, and the temperature allowed to rise to 100°. The sulphonation is complete in about 6 hours, when the reaction mixture is transferred to a large basin, diluted with water, and milk of lime added gradually to neutralise the excess acid. The calcium sulphate and any ferric hydroxide present are removed by filtration and washed with hot water. Sodium carbonate is added to the filtrate until just alkaline to phenolphthalein, and the calcium carbonate filtered off. The filtrate is then evaporated almost to dryness, when the sodium salts of *o*- and *p*-sulphonic acids separate out.

*Yield.*—95% theoretical (340 gms.) (total *o* and *p*).

*o*- Crystallises with $2H_2O$; plates. (Am. Soc., 8, 176; B., 12, 1851.)

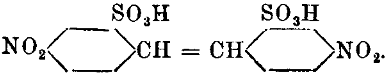
*p*- Crystallises with $4H_2O$; plates or prisms; M.P. 92°. (Am. Soc., 10, 140.)

**Separation of** *o*- **and** *p*-**Toluenesulphonic Acids.**—The mixture prepared above is treated gradually with an equal weight of finely pulverised phosphorus pentachloride. When the reaction is complete, cold water is added, the whole being surrounded by a freezing mixture. The *p*-sulphonyl chloride separates as a solid (M.P. 69°) recrystallisable from alcohol. The *o*-sulphonyl chloride is an oily liquid (M.P. 10°), and is separated from the filtrate by means of a funnel.

$$C_6H_4CH_3SO_3Na + PCl_5 \rightarrow C_6H_4CH_3SO_2Cl + POCl_3 + NaCl.$$

These sulphonyl chlorides form derivatives with primary and secondary amines useful for identification purposes.

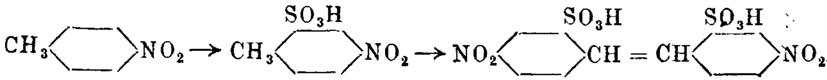
PREPARATION 288.—**4 : 4′ :-Dinitrostilbine-2 : 2′ :-disulphonic Acid (Na Salt).**




$C_{14}H_{10}O_{10}N_2S_2$. 430.

100 gms. *p*-nitrotoluene are sulphonated, as described for nitrobenzene (p. 314), and the sodium salt separated. It is dissolved in 500 c.cs. water at 60° with the addition of sodium carbonate (about 50 gms.). The solution is filtered from iron oxide and made up to 2 litres at 50°. 160 gms. at 35% caustic soda solution are added during $\frac{1}{2}$ hour. No sodium salt should separate out. A mixture of 1,700 gms. sodium hypochlorite solution, containing about 5% NaOCl and 300 gms. of 35% caustic soda

solution, is allowed to drop in during 10 hours. The temperature must not exceed 56°, otherwise yellow dyestuffs are formed. The mixture is allowed to stand at 55° for 24 hours. Free chlorine should be present during the whole period (test with starch potassium iodide paper). It is then cooled to ordinary temperature and 400 gms. salt added. After standing for a day the yellow crystalline sodium salt of the acid is precipitated, and is filtered off and washed with brine.



*Yield.*—About 40% theoretical (60 gms.). Used for preparation of diamido-stilbene-disulphonic acid and stilbene dyestuffs. (B., 30, 3100.)

**Reaction CXLVII. Action of Fuming Sulphuric Acid (oleum) on Hydrocarbons or Substituted Hydrocarbons.**—It is sometimes difficult to introduce a sulphonic group by means of conc. sulphuric acid, and it is then necessary to use fuming acid (*i.e.*, acid containing up to 70% free $SO_3$). The same factors as before have an important influence on the reaction. Usually a high temperature is necessary where more than one $SO_3H$ has to be introduced. In some cases oleum is used in preference to sulphuric acid, in order to reduce the time and the temperature of sulphonation.

**Estimation of $SO_3$ in Oleum.**—The oleum is melted, if necessary, by placing the bottle in warm oil (*caution !*), and a quantity is dropped into the bottom of a clean, dry, tared test tube to a depth of about $1\frac{1}{2}$ inches (8—10 gms.). The whole is weighed, and the weight of oleum obtained by difference. The test tube is now heated and drawn out near its open end and sealed. This is then carefully placed in a graduated litre flask containing about 500 c.cs. of water. The flask is securely stoppered, and the test tube broken by shaking. Shaking is continued till all the white fumes disappear. The flask is then allowed to cool, and its contents made up to 1 litre. 250 c.cs. are then removed and titrated with normal caustic soda solution, using methyl orange as an indicator.

If $W$ = weight of oleum

$n$ = c.cs. of N.NaOH to neutralise W,

$$\text{then } \%\ SO_3 = \frac{4{\cdot}9n - 100W}{{\cdot}225W}.$$

The percentage of $SO_3$ can also be obtained by estimating the total $H_2SO_4$ by titration given by the oleum, reckoned as $H_2SO_4$. The % excess of $H_2SO_4$ over 100, when multiplied by 4·44, gives the percentage of $SO_3$, *e.g.*, if total $H_2SO_4$ = 105% of the oleum, then % $SO_3 = 5 \times 4{\cdot}44 = 22{\cdot}2$.

The results obtained are a little high, as oleum contains a small percentage of $SO_2$. This may be estimated by titrating 250 c.cs. with N/10 iodine solution, using starch as indicator. By subtracting this result from the total obtained by titration with NaOH, the true percentage of $SO_3$ can be calculated.

**Preparation of Oleum of a given Strength.**

1. From two oleums of different strength.

$$\text{oleum} = a\%\ SO_3$$
$$\text{oleum} = c\%\ SO_3$$
$$\text{oleum} = b\%\ SO_3 \text{ required,}$$
$$\text{then } x = \frac{100\,(a-b)}{b-c}$$

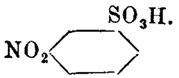
where $x$ = quantity of $c$ to be added to 100 gms. of $a$ to give $b$.

2. From oleum and conc. sulphuric acid.

$$\text{oleum} = a\%\ SO_3$$
$$\text{conc. sulphuric acid} = c\%\ H_2SO_4$$
$$\text{oleum} = b\% \text{ required,}$$
$$\text{then } x = \frac{100\,(a-b)}{444 - 4{\cdot}44c + b}$$

where $x$ = quantity of conc. $H_2SO_4$ to be added to 100 gms. of $a$ to give $b$.

PREPARATION 289.—**Nitrobenzene-*m*-sulphonic Acid.**



$C_6H_5O_5NS$. **203.**

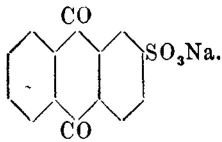
375 gms. oleum (25% $SO_3$) are placed in a cast-iron sulphonation pot and heated to 70°. 123 gms. nitrobenzene are run in carefully. Heat is evolved and the temperature rises up to 100°—110°, and must not be allowed to rise higher. The inflow of nitrobenzene must be slackened, or external cooling applied, if necessary. When all the nitrobenzene has been added, the mixture is heated to 110°—115°, until sulphonation is complete (test). The odour of nitrobenzene should be absent. If the sulphonation is not complete after half an hour, more oleum is added.

The mixture is allowed to cool, and is then poured on to about 500 gms. ice, with good stirring. The sulphonic acid passes into solution. Some sulphone is formed, which may be removed by filtration. 200 gms. common salt are slowly added to the solution, with continuous stirring, when the sodium salt crystallises out, and after standing for about 10 hours is filtered off.

*Yield.*—90—95% theoretical (200—214 gms.). Plates; chloride melts at 60·5°; used for preparation of metanilic acid (see p. 359). (A., 120, 164.)

This process is used in the sulphonation of *p*-nitrochlorobenzene, *p*-nitrotoluene, *o*-nitrochlorobenzene, chlorobenzenes, etc.

PREPARATION 290.—**Anthraquinone-β-Sodium Sulphonate ("Silver Salt").**

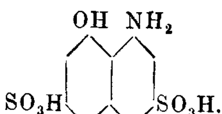


$C_{14}H_7O_5SNa$. 310.

100 gms. dry, finely divided anthraquinone are added cautiously to 150 gms. oleum containing 25% $SO_3$, with continuous stirring, the temperature being kept at 25°—30°. The temperature is then raised to 120° during 4 hours, and then to 140° during a further 2 hours, using an oil bath. The vessel must be kept closed to prevent loss of $SO_3$. After cooling, the mixture is poured into 3 litres of water (*caution!*) and the unchanged anthraquinone filtered off (25—40 gms.). Chalk is added to the filtrate until completely neutralised, and the calcium sulphate filtered off. The calcium in solution is then precipitated as carbonate by adding dilute sodium carbonate (test). It is then filtered and the filtrate evaporated down to about 400 c.cs., and allowed to cool. The sodium salt separates out after standing for about 2 days. It is then filtered and washed with a little water.

*Yield.*—40—60% theoretical (60—90 gms.). Silvery glistening plates; soluble in water; crystallises with $1H_2O$; used for making alizarin (see p. 391). (A., 160, 131; Z. a., 44, 912.)

PREPARATION 291.—**1 : 8-Aminonaphthol-3 : 6-Disulphonic Acid** (*H. acid*)—**Mono-sodium Salt.**



$C_{10}H_9O_7NS_2$. 319.

*Sulphonation.*—1,024 gms. of 24% fuming sulphuric acid (fuming acid of higher strength than this may be diluted with 100% sulphuric acid), or the equivalent of fuming acid of strength 22—24%, are weighed and introduced into a sulphonation pot. The acid is stirred and heat applied until the temperature reaches 100°; 128 gms. of naphthalene are added quickly in portions at a time, and this causes a considerable rise in temperature. When the naphthalene is all in, the temperature is raised to 165°, at which it is maintained for 8 hours, with slow stirring. During this process naphthalene 3.6.8-trisulphonic acid is the chief product formed. After the above time the pot is allowed to cool to room temperature.

*Nitration.*—At room temperature the sulphonation mixture should be capable of being stirred, but if not conc. sulphuric acid must be added until the contents can be stirred. The pot is then placed in a bath, which can be filled with cold water, the agitator is set in motion, and conc. nitric acid slowly run from a dropping funnel to effect nitration. The temperature should be maintained at about 20° during nitration. The theoretical

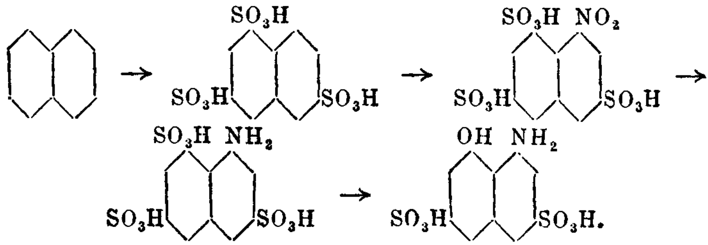
quantity of nitric acid, calculated from the naphthalene used, is necessary, and acid of about 60% is preferable, the strength being ascertained by use of a hydrometer (p. 514).

After the nitric acid has been added, the mixture is allowed to stand at 25° for an hour, and then the temperature is raised to 50° in the course of the next hour. After this time it is poured into 1,500 c.cs. water; volumes of nitrous fumes are given off, and the temperature rises considerably. During this process 1-nitro-3 : 6 : 8-naphthalene-trisulphonic acid is the chief product formed.

*Reduction.*—256 gms. of iron borings are weighed and about 10 gms. of these added to the solution of nitro-sulphonic acid at about 50°; this causes the evolution of nitrous fumes. The remaining iron is added in portions at such a rate that the reduction proceeds briskly; the agitation should be vigorous enough to keep the iron swirling round. After all the iron has been added, agitation is continued for an hour; the temperature is then raised to 50°, 150 gms. of common salt added, and the agitation continued for an hour while the mixture cools. The acid sodium salt of naphthylamine-trisulphonic acid is by this means precipitated; along with any unattacked iron this is filtered off and washed with 10% brine. The contents of the funnel are placed in a vessel and boiled up with water until all the naphthylamine-sulphonic acid dissolves; while still almost boiling the solution is again filtered to separate the iron residue. The filtrate, while still warm, is treated with 15 gms. common salt for each 100 c.cs. volume and agitated while the salt dissolves; before this is complete, separation of the sulphonic acid begins. The mixture is afterwards cooled to 15°, and the purified aminosulphonic acid (Na salt) filtered off. The precipitate is washed on the funnel with 100 c.cs. of 10% brine, pressed in a screw press (p. 33) and dried at 100°. When dry it is ground up, and a sample estimated with standard nitrite (see p. 493); it is generally of 75—80% purity.

*Caustic Fusion.*—This operation is performed in a small autoclave, for manipulation of which see p. 45. 85 gms. caustic soda and 134 c.cs. water are placed in the vessel and heat applied until solution takes place; 128 gms. of naphthylamine-trisulphonic acid (70—80%) are then added, and the lid of the autoclave bolted on. The mixture is gradually heated up to 180° and maintained at this point for 5 hours, the pressure being about 100 lbs. After cooling, the autoclave is opened, allowing any residual pressure to escape gradually—a certain amount of ammonia is always present. The reaction product is introduced into a large beaker or stoneware jar, diluted with 750 c.cs. water, and acidified with conc. hydrochloric, or 50% sulphuric acid; volumes of sulphur dioxide from the decomposition of the sodium sulphite are given off. When testing for acidity, a small sample should be withdrawn and boiled to expel sulphur dioxide, prior to testing with Congo paper. The aminonaphthol-disulphonic acid, which is formed in this reaction, being only very sparingly soluble in solutions of sodium chloride or sulphate, is practically all precipitated as the mono-sodium salt on acidification. After acidification

the mixture is cooled to room temperature and allowed to stand for 1 hour. The precipitate is then filtered off, washed with 100 c.cs. of 10% brine, pressed, and dried at 100°.



*Yield.*—50 gms. of 80—85% purity (see estimation, p. 494). Monosodium salt is soluble in water and crystallises with $1\frac{1}{2}H_2O$; fine needles. (B., 27, 2148; D.R.P., 69722.)

**Reaction CXLVIII. Action of Chlorosulphonic Acid ($Cl.SO_3H$) on Hydrocarbons or Substituted Hydrocarbons.** (B., 42, 2057, 2274).—Chlorosulphonic acid (see p. 511) is used for sulphonating in special cases. See J. C. S., 1932, 715.

$$R.H + Cl.SO_3H \rightarrow R.SO_3H + HCl.$$

The chief advantage in the use of this acid is its selective property, whereby certain sulphonic acids are formed, which could not be formed by direct sulphonation with sulphuric acid or oleum, or which might be formed only in presence of other isomers, the separation of which might be difficult. For example, naphthalene sulphonated with oleum at the ordinary temperature gives a mixture of 1 : 5- and 1 : 6-disulphonic acids, while chlorosulphonic acid yields only the 1 : 5-acid. Similarly, with toluene, chiefly the ortho acid is formed. With excess of chlorosulphonic acid a sulphonyl chloride is formed, except in the case of phenols or naphthols, which give the free sulphonic acid.

$$R.H \rightarrow R.SO_2OH \rightarrow R.SO_2Cl.$$

When chlorosulphonic acid reacts with amides, acid chlorides are formed, while amines yield sulphamic acids.

$$SO_3HCl + 3C_6H_5NH_2 \rightarrow C_6H_5NH.SO_3H.C_6H_5NH_3 + C_6H_5NH_2.HCl.$$

When the sulphonic acid produced by the interaction of chlorosulphonic acid has to be nitrated afterwards, it must be isolated previous to nitration, otherwise the chlorine liberated may form chloro-derivatives.

PREPARATION 292.—"**Saccharin**" (*o-Benzoicsulphinide*).

$$C_6H_4\left\langle\begin{matrix} CO \\ SO_2 \end{matrix}\right\rangle NH. \quad C_7H_5O_3NS. \quad 183.$$

1. *Toluene-o-sulphonyl-chloride.*—100 gms. pure toluene are slowly run into 500 gms. of chloro-sulphonic acid cooled to 0° in a pot fitted with good mechanical agitation, the temperature during the addition being kept at 0°—5°. When all the toluene has been added stirring is continued for about 12 hours at the same temperature. The mass is then poured

on to ice, when an oily layer separates. The liquid ortho-sulphonyl chloride, which usually contains some of the solid para-compound, is then separated and, after further treatment with ice and salt, is filtered and the ortho-compound separated from the salt solution in a funnel.

The pot in which the sulphonation is carried out should have an exit tube for the escape of HCl, which may be absorbed in fuming sulphuric acid with the formation of more chlorosulphonic acid.

$$C_6H_5CH_3 \rightarrow C_6H_4\begin{cases} CH_3 \\ SO_2Cl. \end{cases}$$

*Yield.*—Ortho 85% theoretical (110 gms.). (E.P., 25273, 1894.)

2. *Toluene-*o*-sulphonamide.*—The *o*-sulphonyl chloride is gradually added to an equal quantity of 20% ammonia solution, which is cooled in a freezing mixture. When all has been added, the reaction is completed by removing the freezing mixture and gently heating. The sulphonamide is then filtered off and dissolved in N. caustic soda solution, filtered, and reprecipitated by adding sufficient hydrochloric or sulphuric acid to precipitate 75% of the amide in solution. The precipitate is redissolved by heating, and almost pure *o*-sulphonamide crystallises out on cooling (M.P. 133°—134°).

$$C_6H_4\begin{cases} CH_3 \\ SO_2Cl \end{cases} \rightarrow C_6H_4\begin{cases} CH_3 \\ SO_2NH_2. \end{cases}$$

(E.P., 22726, 1894; 3930, 1895; 848, 1903; D.R.P., 133919.)

3. *Saccharin.*—One equivalent of the *o*-sulphonamide (171 gms.) is dissolved in one equivalent of caustic soda (40 gms.) and 2,565 gms. of water. This is heated to 40°—50°, and 256 gms. of solid potassium permanganate are slowly added with stirring. When all the permanganate has been added and the colour has almost disappeared, a little NaHS is added to decolorise, and the precipitated manganese compound filtered off and washed with water until acid added to the filtrate gives no precipitate of saccharin. The combined filtrate and washings are then cooled down to ordinary temperature and neutralised with hydrochloric acid, using methyl orange as indicator. This treatment precipitates unchanged *o*-sulphonamide, which is filtered off. Hydrochloric acid is then added to the filtrate, and the precipitated saccharin filtered off, washed with water, and dried at 40°.

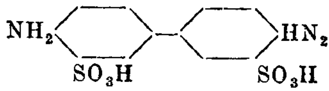
$$C_6H_4\begin{cases} CH_3 \\ SO_2NH_2 \end{cases} \rightarrow C_6H_4\begin{cases} CO \\ SO_2 \end{cases}\!\!NH.$$

White crystalline powder; M.P. 220°; soluble in hot water and in alcohol, and in alkalis or alkali carbonates with formation of salts. About 500 times sweeter than cane sugar. (E.P., 3563, 1903.)

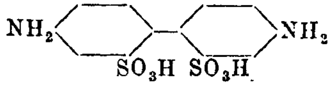
**Reaction CXLIX. Intramolecular Rearrangement of Aromatic Amine Sulphates.**—When sulphuric acid is added to an amine a sulphate is usually formed. If the sulphate is heated either alone (baking process) or with

excess of conc. sulphuric acid, a rearrangement takes place, the sulphonic group entering the *p*-position to the basic group.


Sulphonic acids can be made by the baking process, which are difficult to make in the ordinary way, *e.g.*,

By ordinary process →


(*a*)

By baking process →


(*b*)

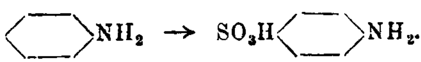
(*a*) yields cotton dyestuffs, while (*b*) yields wool dyestuffs.

In the baking process much less sulphuric acid is required. For new method of eliminating water, see E.P., 354,201.

PREPARATION 293.—**Sulphanilic Acid** (1-*Amino*-4-*benzenesulphonic Acid*).

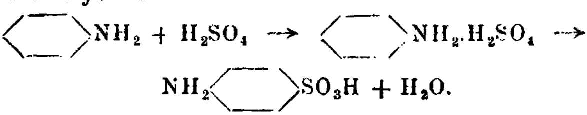
$C_6H_7O_3NS$. 173.

*Method I.*—20 gms. of aniline are gradually added to 65 gms. of conc. sulphuric acid placed in a round-bottomed flask. Much heat is developed, and the contents of the flask should be cooled when the aniline is being added. The flask which contains aniline sulphate and excess conc. sulphuric acid is now heated on an oil or paraffin bath to 185° for about 5 hours. When a test portion, treated with dilute caustic soda solution, liberates no free aniline, the sulphonation is complete. The contents of the flask, after cooling, are poured into cold water, when the sulphanilic acid separates, usually as discoloured crystals. These are filtered off and recrystallised from water, adding a little animal charcoal, if necessary. A further crop can be obtained from the mother liquor.



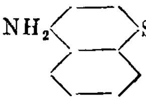

*Yield.*—55% theoretical (20 gms.).

*Method II.* (baking process).—93 gms. of aniline are placed in a basin and 105 gms. of conc. sulphuric acid gradually added in a stream, with good agitation. The hot paste is then spread on a lead tray and placed in an air oven at 190°—200° for 8 hours. The cake is now ground up and boiled for some time with water to which some caustic soda has been added till alkaline, to remove the unchanged aniline present (about 3%). It is then filtered through a cotton filter, and the acid is obtained by adding sulphuric acid to the filtrate until acid to Congo paper. If the acid is discoloured it may be boiled up with animal charcoal, filtered, and allowed to crystallise.



*Yield*.—90% theoretical (155 gms.). Rhombic crystals; does not melt; forms two hydrates; + $2H_2O$ when crystallised below 20°; + $1H_2O$ when crystallised between 20°—44°; important intermediate for dyestuffs. (A., 100, 163; Z. a., 9, 685.)

PREPARATION 294.—**Naphthionic Acid** (1-*Naphthylamine*-4-*sulphonic acid*).

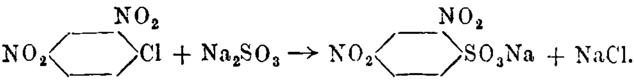



$C_{10}H_9O_3NS$. 223.

The process is similar to that used for sulphanilic acid. 70 gms. of α-naphthylamine and 50 gms. of conc. sulphuric acid are used. Before the paste is spread on the tray it is mixed with about 3 gms. of oxalic acid. It is then placed in the oven and heated, as before. When the mass has been cooled and powdered, it is boiled up with water and neutralised with milk of lime (test) and filtered. The acid is obtained by acidifying the filtrate with hydrochloric acid.

*Yield*.—80—85% theoretical (88—94 gms.). Crystallises with $\frac{1}{2}H_2O$; used largely in preparation of azo dyestuffs. (B., 13, 1948; 19, 578; Z. a., 9, 685.)

**Reaction CL. Action of Sulphites and Bisulphites on Substituted Hydrocarbons.**—(*a*) Metallic sulphites and bisulphites are used in certain cases for introducing the $SO_3H$ group, and especially to replace halogens where the halogen is in the nucleus, and *ortho* to a $NO_2$, $SO_3H$ or CHO group.




(*b*) In some cases reduction takes place simultaneously with sulphonation, *e.g.*, *m*-dinitrobenzene gives *m*-nitroaniline sulphonic acid and nitrobenzene diazonium chloride gives *p*-nitrophenylhydrazine sulphonic acid.

(*c*) The same reagents are used for the formation of alkyl sulphonic acids by interaction with alkyl halides.

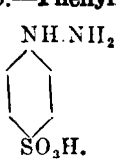
$$C_2H_5I + Na_2SO_3 \longrightarrow C_2H_5SO_3Na + NaI.$$

Halogens in the side chain of aromatic compounds also undergo this reaction.

(*d*) With certain olefinic compounds, additive compounds are formed.

$$R.CH = CH.COOH + K_2SO_3 \longrightarrow R.CH_2CH(COOH)SO_3K.$$

PREPARATION 295.—**Phenylhydrazine-*p*-sulphonic Acid.**

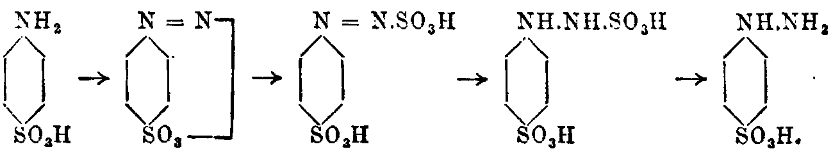



$C_6H_8O_3N_2S$. 188.

51 gms. sulphanilic acid (100%) are dissolved in 200 c.cs. water and 16 gms. caustic soda. Any aniline which may be present is boiled off.

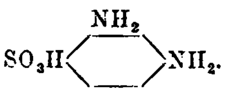
The solution is filtered and cooled, and 35 gms. conc. sulphuric acid are added. The whole is then cooled to 12° (external cooling), and treated with a solution of 21 gms. sodium nitrite in 50 c.cs. water during ½ hour with continuous stirring until a distinct and permanent reaction is given with starch-iodide paper. The diazo sulphanilic acid separates out as fine crystals, which are filtered off, but not dried.

The moist diazo acid is then added to a mixture of 130 gms. bisulphite solution (containing 25% $SO_2$) and enough 35% caustic soda solution to give a distinct alkaline reaction with phenolphthalein to the sulphite solution (25—45 gms. may be necessary). The temperature of the mixture is kept at 45°—50° by placing the vessel in ice-water and stirring. The diazo sulphanilic acid is at once converted into the sulpho-phenyl azo sulphonic acid, which is allowed to stand for an hour. The yellow solution is heated to boiling, and then about 250 gms. conc. hydrochloric acid are added until reaction is strongly acid. This reaction should be performed in a fume cupboard. The reduction takes place by means of the $SO_2$ produced. If the solution does not become decolorised a little zinc dust may be added. The phenylhydrazine sulphonic acid crystallises out on standing. It is filtered and washed with a little water.



*Yield.*—90% theoretical (47 gms.). Crystallises with $\frac{1}{2}H_2O$; soluble in hot water; alkali salts readily soluble; important intermediate for dyes. (B., 18, 3172: A., 190, 69.)

PREPARATION 296.—***m*-Phenylenediamine-4-sulphonic Acid.**



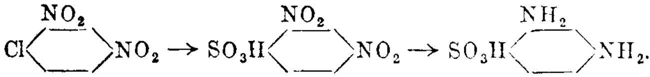
$C_6H_8O_3N_2S$. 188.

101 gms. dinitrochlorobenzene are dissolved in 250 c.cs. of methylated spirits. To this is added 40 gms. $SO_2$, in the form of a conc. solution of sodium sulphite—about 160 gms. $NaHSO_3$, containing 25% $SO_2$ mixed with 50 gms. 40% NaOH until alkaline to phenolphthalein. The sulphite may separate out, even when the mixture is hot, but this is of no consequence. The mixture is heated on the water bath to boiling for 5 hours with good stirring. The product is then cooled, and the sodium salt of the dinitrobenzene sulphonic acid separates in glistening, yellow leaflets.

The sodium salt is then reduced, as in the preparation of *m*-phenylene diamine (see p. 358).

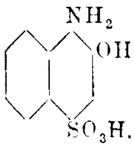
The solution of the diamine sulphonic acid is evaporated down to about 200 c.cs. and 50 gms. common salt added. It is then just acidified with

HCl (Congo paper should be turned only faint violet), and the free acid crystallises out. It is filtered and washed with very little water.



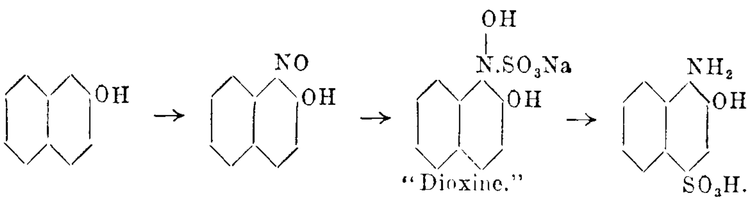

*Yield.*—65% theoretical (61 gms.). Dimorphous; α-form, monoclinic plates; β-form, triclinic prisms; calcium and barium salts easily soluble in water. (A., 205, 104.)

PREPARATION 297.—**1 : 2 : 4-Aminonaphtholsulphonic Acid.**




$C_{10}H_9O_4NS$. 239.

100 gms. of β-naphthol are converted into the corresponding nitroso-naphthol (see preparation, p. 284). The moist nitroso-naphthol is stirred up with a little water and cooled to 5° with ice. To the paste 260 gms. sodium bisulphite solution, containing25 % $SO_2$, are quickly added. The nitroso-naphthol goes into solution after a few minutes; a small quantity of dilute caustic soda can be cautiously added, if necessary. The solution is filtered to remove resinous matter. The filtered solution is treated at 25° with 100 gms. conc. sulphuric acid, which has been diluted with 200 gms. of water. The solution should then give a strongly acid reaction. It is allowed to stand for 1 hour, and it is then warmed to 50° and left overnight—it solidifies to a solid cake. It is filtered off and washed well with water.




*Yield.*—90% theoretical (149 gms.). Almost insoluble in cold water, sparingly soluble in hot; sodium salt sparingly soluble in hot water (B., 27, 23.) See also O. S., XI., 12.

PREPARATION 298.—**Phenylsulphopropionic Acid** [2-*Sulphonic acid of 3-phenylpropan acid*] (**K salt**).

$C_6H_5.CH_2CH.(COOH)(SO_3K)$. $C_9H_9O_5SK$. 268.

15 gms. (1 mol.) of cinnamic acid and 13 gms. (1 mol.) of normal potassium sulphite are refluxed with 280 c.cs. of water for 12 hours, then allowed to cool, and acidified with acetic acid. A crystalline precipitate of phenylsulphopropionic acid separates, which is filtered off and recrystallised from water. A further yield may be obtained by evaporating the

filtrate to dryness, extracting the potassium acetate with hot alcohol, and crystallising the residue of phenylsulphopropionic acid from water.

$$C_6H_5CH : CH.COOH + K_2SO_3 + CH_3.COOH \rightarrow C_6H_5CH_2.CH(COOH)(SO_3K) + CH_3COOK.$$

Needles; melts and decomposes on heating; soluble in hot water. (A., 154, 63.)

PREPARATION 299.—**Ethylsulphonic Acid (Ba salt).**

$$CH_3 CH_2.SO_3H. \qquad C_2H_6O_3S. \qquad 110.$$

20 gms. (2 mols.) of ethyl iodide are boiled under reflux with a solution of 20 gms. (excess) of crystallised ammonium sulphite in 40 c.cs. of water until all goes into solution (6 hours). 100 c.cs. of water are added, and the solution boiled with 30 gms. (excess) of lead oxide until all ammonia is expelled. The lead salt of ethylsulphonic acid and lead iodide are formed; the latter is removed by filtration after the solution cools. Sulphuretted hydrogen is passed into the filtrate until no more lead sulphide—from the decomposition of the lead salt of ethylsulphonic acid—is formed. Lead sulphide is filtered off, and the filtrate neutralised by the addition of excess (20 gms.) of barium carbonate. After filtration, the filtrate containing barium ethylsulphonate is evaporated.

$$2C_2H_5I + 2(NH_4)_2SO_3 + 2H_2O \rightarrow 2C_2H_5SO_2OH + 2NH_4OH + 2NH_4I.$$

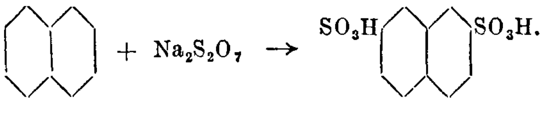
$$2C_2H_5SO_2OH \xrightarrow{PbO} (C_2H_5SO_2O)_2Pb \xrightarrow{H_2S} 2C_2H_5SO_2OH \longrightarrow (C_2H_5SO_2O)_2Ba.$$

*Yield.*—90% theoretical (22 gms.). (A., 168, 146.)

The free acid is stable and forms a deliquescent crystalline mass (B., 15, 445.)

**Reaction CLI. Action of Polysulphates on certain Hydrocarbons.**—The $SO_3H$ group may be introduced in certain cases by the use of potassium trihydrogen disulphate, $KH_3(SO_4)_2$, or sodium pyrosulphate, $Na_2S_2O_7$.

$$C_6H_6 + KH_3(SO_4)_2 \rightarrow C_6H_5SO_3H + KHSO_4 + H_2O.$$




In the anthraquinone series $NaHSO_4$ may be used.

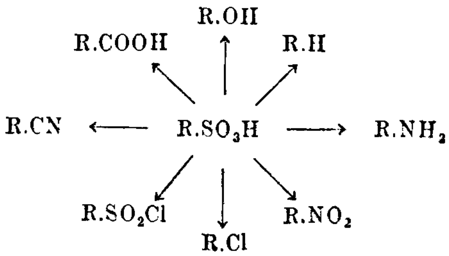
PREPARATION 300.—**Benzenesulphonic Acid.**

20 gms. of benzene and 50 gms. potassium polysulphate are heated under a reflux until all the benzene has dissolved. The cold product is dissolved in water and neutralised with milk of lime and isolated as before.

$$C_6H_6 + KH_3(SO_4)_2 \rightarrow C_6H_5SO_3H + KHSO_4 + H_2O.$$

(D.R.P., 113784.)

**Reactions of the Sulphonic Group.**




1. $R.SO_3H + NaOH \rightarrow R.OH.$

2. (*a*) $R.SO_3H + H_2O \xrightarrow[\text{pressure}]{HCl} R.H.$

   (*b*) $R.SO_3H + H^+ + OH' \rightarrow R.H.$

3. (*a*) $R.SO_3H + NH_3 \xrightarrow[\text{pressure}]{NaHSO_3} R.NH_2.$

   (*b*) $R.SO_3H + NaNH_2 \rightarrow R.NH_2.$

4. $R.SO_3H + HNO_3 \rightarrow R.NO_2.$

5. (*a*) $R.SO_3H + Cl \rightarrow R.Cl$ (goes readily if $SO_3H$ in *a*-position).

   (*b*) $R.SO_3H + PCl_5 \rightarrow R.Cl.$

6. $R.SO_3H + PCl_5 \rightarrow R.SO_2Cl.$

7. $R.SO_3Na + NaCN \rightarrow R.CN.$

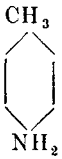
8. $R.SO_3Na + NaCOOH \rightarrow R.COOH.$

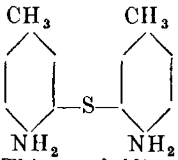
# CHAPTER XXI

## THE LINKING OF SULPHUR TO CARBON (*continued*)

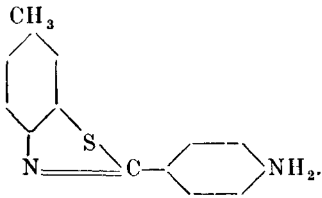
**Reaction CLII. Action of Sulphur and Sodium Sulphide on Aromatic Bases.**—Aromatic amines usually react with sulphur when heated in presence of sodium sulphide to give compounds of complex structure, two nuclei joining together through the *S*-atom. Several compounds are usually formed in the reaction, *e.g.*, *p*-toluidine gives four different products when fused with sulphur. The final products are dyestuffs, some of unknown constitution, and are known as sulphur or sulphide dyestuffs.

The formulæ show the compounds obtained from *p*-toluidine.

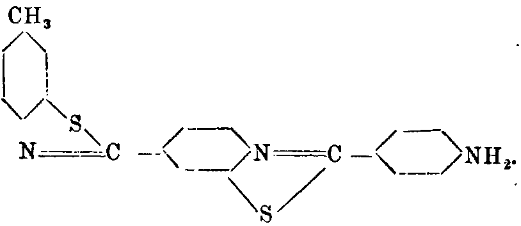




Thio-*p*-toluidine.



Dehydrothio-*p*-toluidine.



*Bis*dehydrothio-*p*-toluidine or Primuline base.

The dyestuffs produced are of various shades; generally speaking, diphenylamines give blue and black dyes, toluidines yellow and brown, and diamines red dyes.

For dyestuff preparations, see Chapter XXVI.

PREPARATION 301.—**Phenthiazine** (*Thiodiphenylamine*).

$$C_6H_4\left\langle\begin{matrix}NH\\S\end{matrix}\right\rangle C_6H_4. \qquad C_{12}H_9NS. \qquad 199.$$

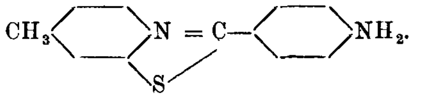
22 gms. of diphenylamine, 8·2 gms. of sulphur, and 3·2 gms. of anhydrous aluminium chloride are melted together. The reaction sets in at 140°—150° with rapid evolution of sulphuretted hydrogen; by lowering the temperature a few degrees the reaction can be slackened. When it has

moderated, the temperature is raised to 160° for a time. The melt, when cool, is ground up and extracted, first with water and then with dilute alcohol. The residue consists of almost pure thiodiphenylamine. It can be recrystallised from alcohol.

$$C_6H_5—NH—C_6H_5 + 2S \rightarrow C_6H_4\left\langle {NH \atop S} \right\rangle C_6H_4 + H_2S.$$

*Yield.*—93% theoretical (23·5 gms.). Yellowish leaflets; M.P. 180°. (D.R.P., 237771.)

PREPARATION 302. — **Dehydrothio-*p*-toluidine** (4′-*amino*-1-*phenyl*-5-*methylbenzothiazole sulphonate*).



$C_{14}H_{12}N_2S$. 240.

107 gms. *p*-toluidine are heated with 70 gms. powdered sulphur (*not* flowers of sulphur) and 1 gm. sodium carbonate (to remove acidic substances in the sulphur) to 180° in a sulphonating pot fitted with a good agitator and reflux condenser. The $H_2S$ which is evolved is absorbed by a tower filled with lumps of moist caustic soda. The temperature is raised to 220° after about 8 hours, by which time the evolution of $H_2S$ slackens, and kept at 220° for 5 hours. The evolution of $H_2S$ now practically ceases, and the melt is then poured on to a tray to solidify.

The yellow crust is then finely ground and extracted with 95% alcohol. This dissolves the toluidine, thiotoluidine, and the dehydrothiotoluidine, leaving the insoluble primuline base (p. 389). The extract is evaporated to dryness and heated to 250°, which removes the toluidine and part of the thiotoluidine. The mixture is then sulphonated with 25% oleum and poured on to ice, filtered, and well washed with water until the washings give only a faint acid reaction. The toluidine and thiotoluidine sulphonic acids pass into solution. The residue is dissolved in 50 gms. of 20% ammonia solution and 800 c.cs. water, and heated to 80°, other 400 c.cs. of water being then added. The solution is filtered hot, if necessary, and the ammonium salt of dehydrothiotoluidine sulphonic acid separates out in the course of 2 days. Primuline can be obtained from the mother liquor by saturating with common salt at the boiling point.

*Yield.*—Ammonium salt, 25 gms.; primuline, 80 gms. Base—needles (from alcohol); M.P. 190°—191°; B.P. 434°; primuline (see p. 389). (B., 22, 333; 22, 424; 25, 1084.)

**Reaction CLIII. Action of Sulphur Dioxide on Aromatic Hydrocarbons in presence of Aluminium Chloride or Mercuric Chloride.** (A. Ch., [6], 14, 443.)

$$C_6H_6 + SO_2 \xrightarrow{AlCl_3} C_6H_5SO_2H.$$

Sulphinates may also be formed by :—

1. Action of $SO_2$ on zinc alkyls.

$$(C_2H_5)_2Zn + 2SO_2 \rightarrow (C_2H_5SO_2)_2Zn.$$

2. Action of zinc on sulphonyl chlorides.

$$2C_2H_5SO_2Cl + 2Zn \rightarrow (C_2H_5SO_2)_2Zn + ZnCl_2.$$

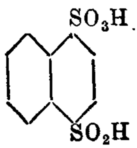
**Reaction CLIV. Action of Sulphur Dioxide on a Diazonium Compound in presence of Finely Divided Copper.** (Gattermann, B., 32, 1136.)

Sulphinic acids are formed in good yield.

$$2R.N_2Cl + 2SO_2 + 2Cu \rightarrow 2R.SO_2H + 2N_2 + Cu_2Cl_2.$$

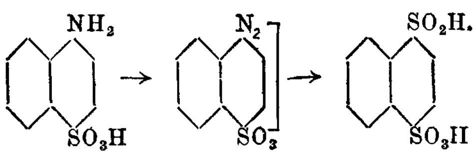
Sulphinic acids are unstable liquids passing readily into sulphonic acids on oxidation with alkaline permanganate. Where a mixture of isomeric sulphonic acids is formed by direct sulphonation the individual sulphonic acids may be prepared by this method from the corresponding sulphonic acids. For example, *o*-toluenesulphonic acid may be prepared from *o*-toluidine.

PREPARATION 303.—**Naphthalene-1 : 4-Sulphonicsulphinic Acid.**



$C_{10}H_8O_5S_2$. 272.

50 gms. sodium naphthionate (see p. 320) are diazotised in the usual way (see p. 372). The diazo-anhydride compound separates. Sulphur dioxide is then passed in until the solution is saturated, the temperature being kept below 0°. Copper powder (see p. 508) is then added very gradually until the evolution of nitrogen ceases, a slow stream of $SO_2$ being passed through during the addition. The whole is then filtered, and common salt is added to saturate the filtrate, when the sodium salt of 1 : 4-sulphonicsulphinic acid separates, and after filtration is recrystallised from water. The free acid may be isolated by passing hydrochloric acid gas into the solution in water of the sodium salt.



*Yield.*—Almost theoretical (62 gms.). (J. C. S., 95, 342.)

**Reaction CLV. Action of Potassium Xanthate on Diazonium Compounds with Subsequent Hydrolysis and Oxidation.** (E.P., 11865, 1892).

$$C_6H_5N_2Cl + KSC{\begin{matrix}\diagup\!\!\diagup S\\ \diagdown OC_2H_5\end{matrix}} \rightarrow C_6H_5SC{\begin{matrix}\diagup\!\!\diagup S\\ \diagdown OC_2H_5\end{matrix}}$$

$$\xrightarrow{H_2O} C_6H_5SH \xrightarrow{O} C_6H_5SO_3H.$$

**Reaction CLVI. Action of Hydrogen Sulphide on Diazonium Compounds.** (B., 29, 272.)

In neutral solution at 0° diazo sulphides are formed, *e.g.*,

$$NO_2C_6H_4N_2Cl \rightarrow (NO_2C_6H_4N_2)_2S.$$

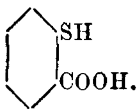
In hydrochloric acid solution the disulphide is ultimately formed—

$$(NO_2C_6H_4N_2)_2S_2.$$

On heating a diazonium solution in presence of hydrogen sulphide, nitrogen is evolved, and a mercaptan is formed—

$$R.N_2Cl + H_2S \rightarrow R.SH.$$

PREPARATION 304. — **Sulphosalicylic Acid** (*Thiophenol-o-carboxylic acid*).



$C_7H_6O_2S$. 154.

10 gms. anthranilic acid (see p. 248) are dissolved in 150 c.cs. water and 5 gms. hydrochloric acid. 20 gms. of ice are added and the whole diazotised in the usual way. $H_2S$ is passed through the diazonium solution until the yellow precipitate becomes red. $C_6H_4(COOH)N_2SH$ is formed, and after filtration the moist precipitate is dissolved in sodium carbonate solution, and heat is applied until a test portion gives a white precipitate with hydrochloric acid. The solution is acidified with hydrochloric acid and the sulphosalicylic acid filtered off and washed with cold water.

Insoluble in water; M.P. 163°—164°; salts amorphous. (D.R.P., 69073; B., 22, 2206; 31, 1666.)

**Reaction CLVIII. Action of Hydrosulphides on Alkyl Halides or Sulphates, or on certain Aromatic Halogen Derivatives.**

$$R.Cl + KSH \rightarrow R.SH + KCl.$$
$$R.HSO_4 + KSH \rightarrow R.SH + KHSO_4.$$

The mercaptans are colourless liquids, mostly insoluble in water, possessing a characteristic disagreeable odour.

Other methods by which mercaptans can be formed are :—

1. Action of KCNS on diazonium salts and subsequent hydrolysis (B., 23, 738).

$$R.N_2Cl \rightarrow R.CNS \rightarrow R.SH.$$

2. Action of KSH on diazonium salts (B., 20, 349).

$$R.N_2Cl \rightarrow R.SH.$$

3. See Reaction CLVI.

PREPARATION 305.—**Sulphosalicylic Acid** (*Thiosalicylic Acid*).

50 gms. *o*-chloro-benzoic acid are dissolved in 38·5 gms. caustic soda solution containing 13·5 gms. caustic soda. 100 gms. of sodium hydrosulphide and 0·5 gm. copper sulphate are then added, and the whole heated with stirring to about 200°. The mass becomes dark red and melts, when the temperature is raised to 250°. It then gradually solidifies. The melt is dissolved in a litre of water and boiled up with animal charcoal, if necessary, and the thiosalicylic acid precipitated from the filtrate by adding hydrochloric acid. (See Preparation 304.)

*Yield.*—Almost theoretical (48 gms.). See O. S., XII., 76.

PREPARATION 306.—**Ethyl Mercaptan** [*Ethanthiol*].

$C_2H_5SH$. $C_2H_6S$. 62.

50 c.cs. conc. sulphuric acid and 50 c.cs. 20% oleum are added to 100 c.cs. 99% alcohol, the temperature being kept below 70°. The mixture is allowed to stand overnight in a freezing mixture, and then poured on to a mixture of ice and 8% sodium carbonate solution, with stirring. The neutral solution is concentrated until a crust of salt forms on the surface. Sodium sulphate separates out on cooling and is filtered off. A 40% solution of caustic potash in water is saturated with $H_2S$, the volume of the solution being $1\frac{1}{2}$ times the volume of the filtrate. This solution of potassium sulphide is then added to the filtrate and the whole gently distilled, when the ethyl mercaptan passes over. It is shaken up with conc. caustic soda solution to separate ethyl sulphide. The ethyl mercaptan, after removing the oil, is precipitated by adding acid to the alkaline solution.

$$C_2H_5OH \rightarrow C_2H_5.HSO_4 \rightarrow C_2H_5.SH.$$

Colourless liquid; almost insoluble in water; offensive odour. B.P. 36°. (A., 34, 25.)

**Reaction CLVIII. Action of Phosphorus Pentasulphide on Acids or Alcohols.**

$$5C_2H_5OH + P_2S_5 \rightarrow C_2H_5SH + P_2O_5.$$
$$5CH_3COOH + P_2S_5 \rightarrow CH_3COSH + P_2O_5.$$

The oxygen is replaced by sulphur with the formation of mercaptans and thio-acids.

PREPARATION 307.—**Thioacetic Acid.**

$CH_3COSH$. $C_2H_4OS$. 76.

150 gms. of phosphorus pentasulphide are ground up and mixed with an equal weight of glacial acetic acid and 50 gms. of glass beads. The whole is placed in a distilling tank of at least 1 litre capacity, fitted with a condenser and a thermometer, and continuously warmed with a naked flame. Heating is stopped as soon as the reaction begins, which is allowed to proceed spontaneously, heat being applied when it moderates. Much frothing may take place. The reaction is stopped when the thermometer reaches 103° and the product fractionated.

*Yield.*—25% theoretical (47·5 gms.). Evil-smelling liquid, decomposed by water; B.P. 93°. (B., 28, 1205.)

**Reaction CLIX. Action of Sulphonyl Chlorides on Hydrocarbons in presence of Aluminium Chloride.** (B., 26, 2940.)

$$R.SO_2Cl + C_6H_6 \xrightarrow{AlCl_3} R.SO_2.C_6H_5 + HCl.$$

The compounds formed are termed sulphones; they are also formed by the action of conc. and fuming sulphuric acid on hydrocarbons (see p. 313), and by heating aromatic sulphonic acids with an aromatic hydrocarbon in presence of a dehydrating agent, such as $P_2O_5$.

$$R.SO_2OH + C_6H_6 \xrightarrow{P_2O_5} R.SO_2.C_6H_5.$$

The interaction of halogen compounds and the salts of sulphinic acids yields the same products.

$$R.SO_2Na + BrC_6H_5 \longrightarrow R.SO_2C_6H_5 + NaBr.$$

The sulphones are inert compounds, and are of little importance.

**Reaction CLX. Action of Phosphorus Pentasulphide on Ethers.** (B., 27, 1239.)

Thio-ethers are obtained according to the equation :

$$5(C_2H_5)_2O + P_2S_5 \longrightarrow 5(C_2H_5)_2S + P_2O_5.$$

The thio-ethers are neutral volatile compounds of little importance.

**Reaction CLXI. Action of Sodium or Potassium Sulphide on Alkyl Halides or Alkyl Sulphates.** (B., 27, 1239.)

Thio-ethers are obtained.

$$2C_2H_5I + K_2S \longrightarrow (C_2H_5)_2S + 2KI.$$
$$2C_2H_5.SO_4K + K_2S \longrightarrow (C_2H_5)_2S + 2K_2SO_4.$$

## CHAPTER XXII

### THE LINKING OF HALOGEN TO CARBON

**Reaction CLXII. Replacement of Oxygen and Hydroxyl by Halogens.**—The oxygen of ketone and aldehyde groups is readily replaced by halogen under the influence of phosphorus trichloride or pentachloride; the reaction may be carried out with or without a solvent; solvents commonly employed are chloroform, benzene, petroleum ether, acetyl chloride and phosphorus oxychloride.

Alcoholic hydroxyl may be replaced by halogen:—

(*a*) With halogen acids.

The action is slow with hydrochloric acid, heating under pressure or the use of a dehydrating agent being usually necessary. Hydrobromic acid reacts more easily and hydriodic still more easily. Instead of the acids, bromine and iodine may be allowed to act on the alcohols in presence of phosphorus. For summary, see A. C. R., 1934, 119.

(*b*) With phosphorus oxychloride, phosphorus pentachloride, phosphorus trichloride or tribromide, or sulphur monochloride.

The pentachloride, trichloride and tribromide of phosphorus are also used for replacing hydroxyl by halogen in phenols, carboxylic acids and sulphonic acids. The use of phosphorus trichloride is to be preferred in the preparation of many acid chlorides, since three molecules of acid chloride are then formed per molecule of phosphorus halide, as against one molecule of acid chloride when the pentachloride is used:

$$3R.COOH + PCl_3 \rightarrow 3R.CO.Cl + H_3PO_3$$
$$R.COOH + PCl_5 \rightarrow R.CO.Cl + POCl_3 + HCl$$

and further, no volatile compound of phosphorus is formed. Phosphorus tribromide, and not the pentabromide, is generally used for the preparation of acid bromides. Thionyl chloride does not react with aldehydic and ketonic groups, but reacts readily with carboxyl groups, and sometimes with alcoholic hydroxyl groups (J. S. C. I., 45, 36, 55; Am. Soc., 50, 145; O. S., XIII., 32).

$$2R.COOH + SOCl_2 \rightarrow 2RCOCl + SO_2 + H_2O.$$

Excess of the reagent ($SOCl_2$), without solvent, is generally employed, and the excess removed by distillation or by treatment with formic acid.

Other compounds used for replacing hydroxyl by halogen are carbonyl chloride, benzenesulphonyl chloride and sulphuryl chloride.

PREPARATION 308.—**Benzophenone Chloride** (*Diphenyldichloromethane*).

$(C_6H_5)_2CCl_2$. $C_{13}H_{10}Cl_2$. 237.

24 gms. (1 mol.) of benzophenone are refluxed with 40 gms. (excess) of phosphorus pentachloride on an oil bath at 220°—240° for 4 hours. The

mixture is fractionally distilled under reduced pressure, the fraction boiling at 193° at 30 mms. being retained. It is redistilled under reduced pressure.

$$(C_6H_5)_2CO + 2PCl_5 = (C_6H_5)_2CCl_2 + POCl_3.$$

Colourless oil; B.P. $^{30}$ 193°; B.P. $^{760}$ 305°, with decomposition; D. $^{18.5}_{4}$ 1·235. (B., 3, 752; 29, 2944.)

PREPARATION 309.—**Hippuryl Chloride.**

$C_6H_5.CO\,NH.CH_2.COCl.$ $C_9H_8O_2NCl.$ 197·5.

In this preparation moisture must be excluded as far as possible.

5 gms. (1 mol.) of hippuric acid are finely ground and passed through a fine sieve. The powder is added to a solution of 6·5 gms. (excess) phosphorus pentachloride in 50 gms. of acetyl chloride contained in a strong glass bottle. The bottle is fitted with a good stopper and agitated in a shaking machine for 2 hours. The crystals formed are filtered off, washed with petroleum ether, and dried in a vacuum desiccator containing sulphuric acid. The product may be recrystallised from warm acetyl chloride (*i.e.*, heated on a water bath); a higher temperature, or very prolonged heating, brings about some decomposition.

$$C_6H_5.CO.NH.CH_2.COOH + PCl_5 \rightarrow C_6H_5CO.NH.CH_2.COCl + POCl_3 + HCl.$$

*Yield.*—80% theoretical (4·5 gms.). Colourless needles; becomes yellow at 125°, then dark red, and melts at a higher temperature; with alcohol or water yields hippuric acid. (B., 38, 605.)

PREPARATION 310.—**Benzoyl Chloride** (*Acyl chloride of benzoic acid*).

$C_6H_5COCl.$ $C_7H_5OCl.$ 140·5.

50 gms. (1 mol.) of phosphorus pentachloride are weighed by difference in a fume cupboard into a 250-c.c. distilling flask. 28 gms. (1 mol.) of benzoic acid are added. Dense clouds of hydrogen chloride are evolved during the reaction, and when this is over the contents of the distilling flask are fractionally distilled, the phosphorus oxychloride which passes over about 107° being rejected, and the fraction 190°—200° collected separately.

$$C_6H_5COOH + PCl_5 = C_6H_5COCl + POCl_3 + HCl.$$

*Yield.*—75% theoretical (25 gms.). Colourless liquid; pungent smell; fumes in moist air; B.P. 198·5°; D. $^{19}_{4}$ 1·214. (A., 3, 262; 60, 255.)

PREPARATION 311.—**Acetyl Chloride** [*Ethanyol Chloride*].

$CH_3COCl.$ $C_2H_3OCl.$ 78·5.

50 gms. of glacial acetic acid are placed in a 250-c.c. distilling flask connected by a water condenser with another distilling flask the side of which is fitted with a calcium chloride tube. 40 gms. of phosphorus trichloride are slowly added through a dropping funnel, the distilling flask being cooled in a cold water bath. The bath is then heated at 45° (*caution!*) until the evolution of hydrogen chloride diminishes, after which it is heated to boiling till nothing further distils. The acetyl chloride contains some phosphorus trichloride, so it is redistilled from the collecting

flask over fused sodium acetate (about 3 gms.), the fraction 53°—56° being separately collected in the same way as before.

$$3CH_3COOH + PCl_3 = 3CH_3COCl + H_3PO_3.$$

*Yield.*—55% theoretical, calculated on acetic acid taken (35 gms.). Colourless, pungent smelling liquid; fumes in moist air; B.P. 55°; $D._4^{20}$ 1·105. (A. Ch., [3], 37, 285; C. r., 40, 944; 42, 224.)

The presence of phosphorus trichloride in the first distillate may be proved by adding a few drops of water to a drop of the distillate (*caution!*), oxidising the phosphorus acid formed to phosphoric acid by boiling with nitric acid, and the testing with ammonium molybdate. The acetyl-phosphorus acid remaining in the residue from the second distillation can be proved to be present by evaporating with water on a water bath till the smell of acetic acid disappears, and then testing for phosphoric acid after treatment with nitric acid.

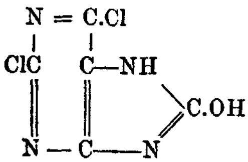
PREPARATION 312.—***p*-Nitrobenzoyl Chloride.**

$NO_2C_6H_4COCl$. $C_7H_4O_3NCl$. 185·5.

20 gms. of *p*-nitrobenzoic acid and 25 gms. of phosphorus pentachloride are mixed in a 200-c.c. flask fitted with a reflux air condenser in a fume cupboard. The flask is heated on a water bath with occasional shaking until the evolution of hydrogen chloride nearly ceases and a clear homogeneous liquid is obtained. The reaction product is transferred to a distilling flask and distilled up to 220° to remove phosphorus oxychloride. The residue of *p*-nitrobenzoyl chloride may be purified by crystallisation from carbon tetrachloride or by distillation under reduced pressure. (B.P.[20] 155°.)

*Yield.*—90% theoretical (20 gms.). Yellow needles; M.P. 73°. Important reagent for identification of alcohols. (O. S., III., 75.)

PREPARATION 313.—**2 : 6-Dichlorouric Acid** (2 : 6-*Dichloro*-8-*hydroxypurine*).



$C_5H_2ON_4Cl_2$. 205.

20 gms. (3 mols.) of dry potassium urate and 24 gms. (excess) of phosphorus oxychloride are heated in a sealed tube for 6 hours at 160°—170°. When cold, the tube is carefully opened and the product poured into water. The precipitate formed is filtered off, dried and powdered. It is then added slowly to 5 parts of conc. nitric acid and boiled for 20 minutes. Only a small portion of the dichlorouric acid goes into solution, and this is reprecipitated by diluting with water. The crude acid is collected, well washed with water, and while suspended in 24 parts of boiling alcohol is treated with ammonia solution until all save a slight impurity is dissolved. Animal charcoal is added and the whole boiled and filtered.

The ammonium salt of the acid separates out in pale yellow leaflets on cooling, and further crops may be obtained by concentrating the mother liquors. The salt is redissolved in water, and the free acid obtained by precipitation with mineral acid.

$$3C_5H_4O_3N_4 + 2POCl_3 \longrightarrow 3C_5H_2ON_4Cl_2 + 2H_3PO_4.$$

*Yield.*—35% theoretical (7 gms.). Colourless crystalline powder which does not melt. (B., 30, 2208.)

PREPARATION 314.—**Diphenylchloroacetic Acid** [*Diphenylchloroethan Acid*].

$(C_6H_5)_2C(Cl).COOH.$ $C_{14}H_{11}O_2Cl.$ 246·5.

15 gms. (1 mol.) benzilic acid and 15 gms. (excess) phosphorus oxychloride are gently warmed together until a slight red colour appears. The melt is then cooled and shaken with a litre of cold water until (1—2 hours) the product becomes quite solid. It is then filtered off, washed with water and dried. It is purified by recrystallisation from a mixture of benzene and petroleum ether.

$$3(C_6H_5)_2C(OH).COOH + POCl_3 \longrightarrow 3(C_6H_5)_2C(Cl)COOH + H_3PO_4.$$

*Yield.*—65% theoretical (11 gms.). Rhombic plates; M.P. 118°—119°, with decomposition. (B., 36, 145.)

PREPARATION 315.—**β-Iodopropionic Acid** [3-*Iodo-pentan acid*].

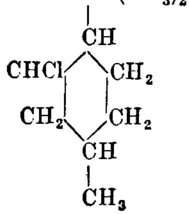
$CH_2I.CH_2.COOH.$ $C_3H_5O_2I.$ 200.

100 gms. (a little more than 1 mol.) of phosphorus di-iodide (see p. 511) are added in small quantities to 52 c.cs. (2 mols.) of glyceric acid (D. 1·26) in a large round flask, and the mixture gently heated till a violent reaction sets in. Should it become too violent the flask is cooled in water. The product, a dark brown syrupy liquid, is again heated, when a second less violent reaction occurs. A light yellow liquid, which, on cooling, solidifies to a crystalline mass, is formed. From this, iodopropionic acid is extracted with hot carbon disulphide (*caution!*) or petroleum ether (*caution!*). The solvent is distilled off and the discoloured residue recrystallised from carbon disulphide or petroleum ether.

$$CH_2(OH).CH(OH).COOH + 3HI = CH_2I.CH_2.COOH + 2H_2O + I_2.$$

Colourless pearly laminæ; slightly soluble in cold, readily in hot water and in alcohol; M.P. 83·5°. (A., 131, 323; 166, 1; B., 9, 1902.)

PREPARATION 316.—**Menthyl Chloride** (1-*Methyl*-4-iso*propyl*-3-*chloro*-cyclo*hexane*).



$C_{10}H_{19}Cl.$ 174·5.

50 gms. (1 mol.) phosphorus pentachloride are covered with dry petroleum ether in a flask and the whole well cooled in ice. 50 gms. (excess) of menthol are added in small portions to the cooled mixture, no fresh menthol being added until the evolution of hydrochloric acid has ceased. The petroleum ether is then distilled off, and the residue distilled with the aid of a fractionating column; crude menthyl chloride passes over at 205°—215°, and it may be purified by redistilling several times. In the crude state it may be used for Preparation 444.

$$C_{10}H_{19}OH + PCl_5 \longrightarrow C_{10}H_{19}Cl + POCl_3 + HCl.$$

*Yield.*—55% theoretical (30 gms.). B.P. 209·5°—210·5°. (B., 29, 317; 25, 686; J. C. S., 41, 54.)

PREPARATION 317.—**Glyceryl mono- and di-chlorohydrins.**

| | | |
|---|---|---|
| $CH_2OH.CH(OH).CH_2Cl.$ | $C_3H_7O_2Cl.$ | 110·5. |
| $CH_2Cl.CH(OH).CH_2Cl.$ | $C_3H_6OCl_2.$ | 129. |

*α-Monochlorohydrin.*—100 gms. glycerine (previously dehydrated by heating to 175° on a sand bath) are cooled, mixed with 2 gms. glacial acetic acid in a flask provided with a two-holed stopper, and the whole weighed. A stream of hydrogen chloride, passed through conc. sulphuric acid and through an empty safety flask, is then led through the mixture, which is heated by an oil bath kept at 100°—110°. The absorption of the gas is very rapid, and when 30% increase in weight has occurred the passage of the gas is stopped. Crude monochlorohydrin is obtained by distilling the product under reduced pressure; and it may be purified by redistillation in this way.

*Yield of Crude.*—86% theoretical (100 gms.). B.P. $^{1}$ 98°—100°; B.P. $^{40}$ 141°. Colourless liquid.

*αγ*-Dichlorohydrin.—*Method I.*—If the passage of the gas is continued beyond the monochlorohydrin stage absorption continues at a slower rate. The temperature of the oil bath should be raised to 130° and the operation continued until an increase, 25% in excess of the theoretical amount, has taken place (allowing for complete volatilisation of the water formed). Fractional distillation under reduced pressure of the product gives an 82% theoretical yield of relatively pure compound. Alternatively the product may be washed with small quantities of water and solid sodium carbonate until just alkaline to litmus, about 50 c.cs. water being necessary to dissolve the salt formed. It is then separated in a funnel and fractionated as before mentioned.

Mobile liquid; somewhat soluble in water. B.P. $^{760}$, 176°; B.P. $^{40}$, 92°; B.P. $^{14}$, 70°—73°. (J. S. C. I. (C. & I.), 49, 102; 50, 949, 970.)

*Method II.*—125 gms. (less than 2 mols.) sulphur monochloride (p. 510) are slowly added in small quantities at a time from a tap funnel to 50 gms. of anhydrous glycerol (dehydrated, as in Method I.) contained in a retort fitted with a reflux condenser. The experiment should be conducted in a fume chamber. The retort is occasionally shaken, and the reaction is completed by heating in a boiling brine bath until the evolution of hydrogen chloride from the condenser has almost ceased. The condenser

is then removed and the mass again heated until all sulphur dioxide and hydrogen chloride are expelled. When cold, the semi-solid mass is twice extracted with twice its volume of ether. The ethereal extract is filtered free from sulphur, and the ether removed by distillation on a water bath. The residue is repeatedly fractionated until a fraction of boiling point 175°—178° is obtained.

$$\begin{gathered} CH_2(OH)CH(OH)CH_2(OH) + 2S_2Cl_2 \rightarrow \\ CH_2Cl.CH(OH)CH_2Cl + 2HCl + SO_2 + 3S. \end{gathered}$$

Colourless ethereal liquid; easily soluble in ether; B.P. 176°; D. $^{0}_{4}$ 1·383. (J., 13, 456; A. Spl., I, 221; A., 122, 73; 168, 42.)

PREPARATION 318.—*iso***Propyl Chloride** (2-*chloropropan*).

$$CH_2.CHCl.CH_2. \qquad C_2H_7Cl. \qquad 78{\cdot}5.$$

To a well-cooled mixture of 95 gms. (2 mols.) conc. hydrochloric acid and 135 gms. (2 mols.) anhydrous zinc chloride, 30 gms. *iso*propyl alcohol are added. The mixture is vigorously boiled for 4 hours under reflux. The upper layer is separated after cooling, and gently boiled under reflux in a distilling flask with closed side tube for 30 minutes. A condenser is attached to the side tube and the *iso*propyl chloride distilled. The distillate is washed with water, dried over calcium chloride, and redistilled, the fraction boiling at 36°—38° being collected separately.

$$\begin{array}{lcl} CH_2 & & CH_2 \\ \dot{C}HOH + HCl & \rightarrow & \dot{C}HCl + H_2O \\ \dot{C}H_3 & & \dot{C}H_2 \end{array}$$

*Yield.*—70% theoretical (28 gms.). Colourless liquid; insoluble in water, B.P. 37°; D. $^{20}_{4}$ 0·859. (O. S., V., 28.)

PREPARATION 319.—**Ethyl Bromide** [*Monobromoethan*].

$$CH_2.CH_2.Br. \qquad C_2H_5Br. \qquad 109.$$

*Method I.—A General Method for the Preparation of Alkyl Bromides.*—The details of this preparation are very similar to those given in the general method for the preparation of alkyl iodides (see p. 338). 10 gms. (excess) of red phosphorus and 50 gms. (excess) of ethyl alcohol are placed in a distilling flask, attached to a condenser and receiver. The receiver consists of a Buchner flask, attached by means of a cork to the end of the condenser, its side tube being connected with a soda-lime tower to trap any fumes of hydrobromic acid. A tap funnel containing 65 gms. (5 mols.) of bromine is fixed through a cork in the neck of the distilling flask. The flask is cooled in water, the bromine slowly added, the whole left for several hours, and the contents of the flask then distilled from the water bath at 50°, the receiver being cooled in ice. The distillate is purified as in the preparation of ethyl iodide, given on p. 338.

$$5ROH + P + 5Br = 5R.Br + H_2PO_4 + H_2O.$$

*Yield.*—Almost theoretical (80 gms.). Colourless, highly refractive liquid; characteristic odour; soluble in all the usual organic solvents;

insoluble in water; B.P. $^{760}$ 38·8°; D. $^{18}_{4}$ 1·47; D. $^{0}_{4}$ 1·485. (J., 1857, 441).

*Method II.*—70 gms. of conc. sulphuric acid and 30 gms. of alcohol are mixed in a 500-c.c. distilling flask, cooled under the tap to ordinary temperature, and 100 gms. (1 mol.) of coarsely powdered sodium bromide added. The flask is closed by a cork, and attached to a condenser leading, by means of an adapter, into a 250-c.c. conical flask, which serves as a receiver. Enough water is poured into the latter to close the end of the adapter. The distilling flask is then carefully heated on a sand bath and distillation slowly conducted until no more oil distils, the receiver being meanwhile cooled in ice. Should the reaction mixture threaten to froth over, the flask must be raised from the sand bath for a moment. The ethyl bromide is separated in a funnel, washed with an equal bulk of dilute sodium carbonate solution, and with water, dehydrated over calcium chloride, and distilled on a water bath, the fraction 35°—43° being retained. Ethyl bromide prepared by this method usually contains traces of ether.

$$C_2H_5OH + H_2SO_4 = C_2H_5.H.SO_4 + H_2O.$$
$$C_2H_5.H.SO_4 + NaBr = C_2H_5Br + NaHSO_4.$$

*Yield.*—80% theoretical (50 gms.).

*Method III.*—A mixture of 20 gms. (1 mol.) of ethyl alcohol and 300 gms. (4 mols.) of hydrobromic acid of constant boiling point, 126°, and D. 1·49 (for preparation see p. 506) is gradually heated in a distillation flask or retort connected with a condenser. The heating is continued until no more oily drops pass over. The distillate is then washed, dried, and distilled, as above. Only a small portion of the acid distils over, and if the residue left in the flask is slowly distilled the excess of hydrobromic acid can be obtained in the form of the solution of constant boiling point, and again used.

$$C_2H_5OH + HBr = C_2H_5Br + H_2O.$$

*Yield.*—86% theoretical (41 gms.). (Am. Soc., 38, 640; Bl., [iv.], 9, 134; O. S., VIII., 120.)

PREPARATION 320.—**Ethyl Chloride** [*Monochloroethan*].

$CH_3.CH_2Cl.$ $C_2H_5Cl.$ 64·5.

Dry hydrogen chloride is passed through a trap into 200 gms. of absolute alcohol containing 100 gms. of fused coarsely powdered zinc chloride, in a 500-c.c. round-bottomed flask heated on a water bath, and fitted with an upright condenser, from the top of which the vapour is led into a conical flask containing water. The inlet tube is cut off just above the surface of the water. Thence the vapour passes through a tower filled with soda-lime, and finally into a U-tube surrounded by ice, and fitted with an open tube at its lowest point. The condensed ethyl chloride drops from the bottom of the U-tube, and is collected in a small conical flask standing in ice. The upright condenser returns all alcohol to the flask. The excess of hydrogen chloride which passes on is absorbed by the water in the conical flask, and the remainder removed in the soda-lime tower. A fairly rapid stream of gas must be maintained on starting

or the alcohol will be sucked back into the trap. The passage of the gas is continued until a sufficient quantity of ethyl chloride has been obtained. It must be stored in a well-stoppered bottle, wrapped in a cloth, and placed in an ice chest, but owing to the risk of its breaking the bottle a quantity should only be kept when there is necessity for so doing.

$$C_2H_5OH + HCl = C_2H_5Cl + H_2O.$$

*Yield.*—Almost theoretical (280 gms.). Colourless liquid; characteristic odour; soluble in all the usual organic solvents; insoluble in water; B.P. 12·5°; D. $^0_4$ 0·9214. (A., 150, 216; 174, 372; Z. Ch., 1871, 147.)

PREPARATION 321.—**Methyl Iodide and Ethyl Iodide.**

Methyl iodide $CH_3I$. 142.
Ethyl iodide. $CH_3.CH_2I$. $C_2H_5I$. 156.

*A General Method for the Preparation of Alkyl Iodides.*—36 gms. (excess) of methyl alcohol (52 gms. of ethyl alcohol) are placed in a 500-c.c. flask with an upright condenser, along with 10 gms. (excess) of red phosphorus. 100 gms. (5 mols.) of powdered iodine are slowly added during 1 hour with frequent shaking, the condenser being detached from the flask momentarily during the addition. The latter is cooled in cold water if necessary. The whole is then allowed to stand overnight, or should that time be not available, it is left for 3 hours with occasional shaking, and then gently boiled on a water bath under a reflux condenser for 1 hour. The former method, however, gives the better yield. The contents of the flask are then distilled off on a water bath into a receiver containing water and cooled in ice.

The distillation is continued till the greater part of the liquid has distilled over, and no oily drops are to be seen in the condenser. The residue consisting of a concentrated solution of phosphorus and phosphoric acids in addition to excess of red phosphorus is discarded. The distillate is shaken up with water to remove alcohol, and then with dilute caustic soda to remove free iodine. Enough alkali must be used to render the lower layer of alkyl halide colourless.* The latter is then separated off, dried over granular calcium chloride (6 gms.) and distilled. The preparation should be kept in the dark in a well-stoppered bottle. If exposed to light, iodine slowly separates, but may be prevented from so doing by adding a small quantity of colloidal silver to the liquid.

$$5ROH + P + 5I = 5RI + H_3PO_4 + H_2O.$$

*Yield.*—Almost theoretical (methyl iodide, 110 gms.; ethyl iodide, 120 gms.). Colourless, highly refractive liquids; characteristic odour; B.P.$^{760}$ methyl iodide, 42·8°; B.P.$^{760}$ ethyl iodide, 72·2°; D. $^{15}_4$ methyl iodide 2·27; D. $^0_4$ ethyl iodide 1·975. (A. Ch., [1], 91, 89; [2], 25, 323; 42, 119; A., 126, 250; J. C. S., 117, 1592; O. S., XIII., 60.)

Care should be taken not to raise the temperature too high, as there

* Should difficulty be experienced in freeing the liquid of iodine, addition of a little sodium thiosulphate solution is effective.

is a danger that the red phosphorus may take fire if air leaks in. To avoid this the distillation, if not done on a water bath, is best carried out in a current of carbon dioxide.

**Reaction CLXIII. Addition of Halogen or Halogen Hydride to Unsaturated Compounds.**—Unsaturated compounds readily combine with chlorine, bromine, hydriodic or hydrobromic acid. The addition of iodine or of hydrochloric acid is generally a matter of difficulty. The unsaturated terpenes, however, unite readily with hydrochloric acid. In the addition of halogen hydrides to unsaturated hydrocarbons, the halogen attaches itself to the carbon atom having the lesser amount of hydrogen; with hydrocarbons, containing the group $-C \equiv C-$, two atoms of halogen are fixed to the carbon atom having the lesser number of hydrogens. In the addition of halogen hydrides to unsaturated acids and aldehydes, the halogen generally enters the $\beta$-position.

$$CH_2:CH.COOH + HCl \rightarrow CH_2Cl.CH_2.COOH.$$

In many of these reactions a solvent is employed, either for the purpose of dissolving a substance or for moderating the action of the reagent. The reagent in the gaseous form may be mixed with carbon dioxide or air.

For action of HCl under pressure, see E.P., 375199, and at low temperature, see Rec., 1934, 544.

PREPARATION 322.—**Ethylene Dibromide** [1 : 2-*Dibromoethan*].

$CH_2Br.CH_2Br.$ $C_2H_4Br_2.$ 188.

Ethylene is prepared by gently heating a mixture of 25 gms. ethyl alcohol, 150 gms. conc. sulphuric acid, and a little sand, in a 2-litre round flask on a sand bath till a steady stream of gas is evolved. A mixture of 1 part of alcohol and 2 parts by weight of conc. sulphuric acid is then slowly added through a tap funnel, the lower opening of which has been drawn out somewhat, at such a rate that the gas is constantly evolved without frothing. The gas is purified by passing it through two wash-bottles in series containing dilute caustic soda solution, to which a little phenolphthalein has been added. The wash-bottles are fitted with safety tubes, and their contents must be renewed occasionally, the phenolphthalein serving to show when they are becoming exhausted. The gas is then bubbled slowly through two wash-bottles with ground-glass stoppers, each containing 15 gms. of bromine (1 mol.) and 50 c.cs. of water, and immersed in water, the temperature of which is kept at 20°—25°. Should the contents of the ethylene generating flask char too badly (some charring is inevitable) a fresh supply of gas must be made. When decolorisation of the bromine is complete (several hours) the crude ethylene bromide is washed with dilute caustic soda solution and with water, dried over calcium chloride and distilled, the fraction 130°—132° being collected separately.

$$CH_3CH_2OH \rightarrow CH_2:CH_2 \rightarrow CH_2Br.CH_2Br.$$

*Yield.*—85% theoretical (30 gms.). Colourless oil; insoluble in water; B.P. $^{760}$ 131·5; D. $^{15}_{4}$ 2·19. (A., 168, 64.)

PREPARATION 323.—**Cinnamic Acid Dibromide** [3-*Phenyl*-2 : 3-*dibromo-propan acid*].

$C_6H_5.CHBr.CHBr.COOH$. $C_9H_8O_2Br_2$. 308.

*Method I.*—40 gms. (1 mol.) of finely divided cinnamic acid are spread out on a large clock-glass and placed in a desiccator over concentrated sulphuric acid. A dish containing 45 gms. (slightly more than 1 mol.) of dry bromine is supported on a glass tripod above the cinnamic acid, the desiccator is closed, and allowed to stand until all the bromine has evaporated from the dish, and has been absorbed by the acid (about 3 days). The clock-glass is removed, the product exposed to the air for several hours, weighed in order to make sure that the theoretical amount of bromine has been absorbed, and recrystallised from dilute alcohol.

$$C_6H_5.CH : CH.COOH + Br_2 = C_6H_5CHBr.CHBr.COOH.$$

*Yield.*—Theoretical (90 gms.). Colourless leaflets; M.P. 195° (decomposition). (J. C. S., 83, 669.)

*Method II.*—12·5 gms. (1 mol.) of cinnamic acid are dissolved in 65 c.cs. of anhydrous ether, and the solution cooled to 0° in a freezing mixture. 4·3 c.cs. (1 mol.) of bromine are then slowly added from a burette while all but diffused daylight is excluded, as the reaction is very violent in direct sunlight. The ether is removed on a water bath, and the residue recrystallised from dilute alcohol.

*Yield.*—Theoretical (25 gms.). Colourless leaflets. (A., 195, 140.)

PREPARATION 324.—**Dichlorocinnamic Acid** [3-*Phenyl*-2 : 3-*dichloro-peopan acid*].

$C_6H_5.CHCl.CHCl.COOH$. $C_9H_8O_2Cl_2$. 219.

Direct sunlight or some other source of ultra-violet rays is essential for this preparation (p. 50).

10 gms. of finely ground cinnamic acid are suspended in 80 gms. of freshly distilled carbon disulphide in a *quartz* flask. A stream of dry chlorine gas (p. 505) is passed in until the liquid assumes a greenish-yellow colour. The mixture is alternately shaken until this colour disappears, and resaturated with chlorine gas until an increase in weight of 5 gms. has taken place. The precipitate is filtered off and recrystallised from aqueous alcohol.

$$C_6H_5CH : CH.COOH + Cl_2 \rightarrow C_6H_5CHCl.CHCl.COOH.$$

*Yield.*—90% theoretical (14 gms.). Colourless leaflets; M.P. 162°—164° (slight decomposition). (B., 14, 1867.)

PREPARATION 325.—**β-Phenyl-β-Bromopropionic Acid** [3-*Phenyl*-3-*bromopropan acid*].

$C_6H_5CHBrCH_2COOH$. $C_9H_9O_2Br$. 229.

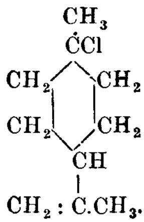
10 gms. (1 mol.) of finely powdered cinnamic acid are heated in a sealed tube (see p. 41) for 2 hours at 100° with 10 gms. of glacial acetic acid which has been saturated with hydrogen bromide at ordinary temperature. (1 gm. of glacial acetic acid dissolves about 0·6 gm. of hydrogen bromide, so there is an excess of the latter present.) The precipitate is recrystallised

from *dry* carbon disulphide (the acid is readily decomposed by water) in which cinnamic acid is readily soluble, even in the cold.

$$C_6H_5CH : CHCOOH + HBr = C_6H_5CHBr—CH_2COOH.$$

Colourless crystals; soluble in hot, slightly soluble in cold carbon disulphide; M.P. 137°. (B., 11, 1221.)

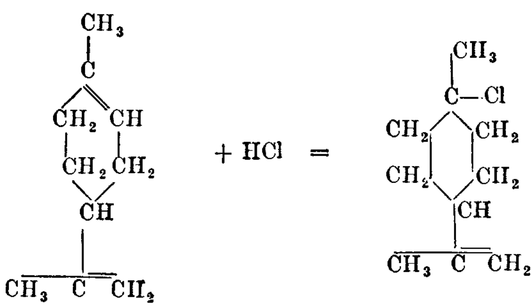
PREPARATION 326.—**Dipentene Hydrochloride** (1-*Chloro-Δ⁸-methene*).



$C_{10}H_{17}Cl$. 172·5.

This reaction must be carried out in a fume cupboard.

20 gms. (1 mol.) of dipentene, which have been *thoroughly* dried over metallic sodium, are dissolved in an equal volume of *dry* carbon disulphide, the solution placed in a dry distilling flask—the side tube of which is connected with a calcium chloride tube—and a current of dry hydrogen chloride (see p. 506) led into the solution through the neck of the flask, which is meanwhile surrounded with ice. After 8 hours the operation is interrupted, the carbon disulphide removed on a water bath, and the residue fractionated under reduced pressure, the fraction 97°—98° at 11—12 mms. being retained.



Colourless liquid; B.P. $^{11}$ 97°—98°.

*Note.*—Every trace of moisture must be excluded in this preparation. (A., 270, 188.)

PREPARATION 327.—**Ethylene Dichloride** [1 : 2-*Dichloroethan*].

$CH_2Cl$
|
$CH_2Cl$. $C_2H_4Cl_2$. 99.

Ethylene is prepared from ethyl alcohol as in Prep. 9 or Prep. 436. The gas is passed first into an empty wash-bottle surrounded by a freezing mixture, and then through a second containing conc. sulphuric acid. The gas is next passed into antimony trichloride at 40°—50°, through

which dry chlorine is also passed. The ethylene dichloride formed is distilled from the antimony trichloride.

Sweet smelling liquid; B.P. 85°. (P. A., 13, 297.)

**Reaction CLXIV. Replacement of Hydrogen by Nascent Halogen.**—When nascent bromine is required, sodium bromide and bromate are added to the substance, and the amount of sulphuric acid required by the following equation is added:—

$$5NaBr + NaBrO_3 + 6H_2SO_4 \rightarrow 6NaHSO_4 + 3H_2O + 6Br.$$

An excess of bromate and sulphuric acid is often employed to react with the hydrobromic acid formed during the bromination of the substance.

$$R.H + 2Br \rightarrow R.Br + HBr.$$
$$HBrO_3 + 5HBr \rightarrow 6Br + 3H_2O.$$

Nascent chlorine or iodine can be generated from their corresponding salts in a similar manner. For the use of standard bromate in estimations, see p. 500.

PREPARATION 328.—***p*-Chloroacetanilide** (1-*Chloro*-4-*acetaminobenzene*).

$C_8H_8ONCl$. 169·5.

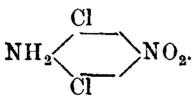
20 gms. of alcohol and 20 gms. glacial acetic acid are mixed, and to this is added 10 gms. (1 mol.) of acetanilide, which is dissolved by gentle heat. After 20 c.cs. of water have been added the solution is heated to 50°, when 200 c.cs. of a cold 10% solution (a slight excess) of bleaching powder are added gradually with continuous stirring. A white precipitate is formed which is filtered off, washed with water, and then recrystallised from alcohol, animal charcoal being added, if necessary. N-Chloroacetanilide is formed as an intermediate product.

$$C_6H_5NH.COCH_3 \xrightarrow{Cl_2} C_6H_5NCl.COCH_3 \rightarrow ClC_6H_4NH.COCH_3.$$

Colourless needles; M.P. 179°—180°; soluble in alcohol, ether, and carbon disulphide. (G., 28, II., 313.)

N-Chloroanilides (J. C. S., 99, 1185; 1928, 998), and dibromodimethyldihydroresorcinol (J. C. S., 121, 1896), may be employed as unique halogenating agents.

PREPARATION 329.—**2 : 6-Dichloro-4-Nitroaniline.**



$C_6H_4O_2N_2Cl_2$. 207.

35 gms. of *p*-nitroaniline are dissolved in 312 c.cs. conc. hydrochloric acid at 50°. A solution of 20·5 gms. of potassium chlorate in 437 c.cs. of water at about 25° are slowly added. When all the chlorate has been added the solution is diluted with a large quantity of water; the precipitate formed is removed by filtration and well washed. It can be further purified by crystallisation from glacial acid or from a mixture of glacial acetic acid and alcohol.

*Yield.*—87% theoretical (42 gms.). Lemon-yellow needles; M.P. 189°. (B., 36, 4391.)

**Reaction CLXV. Replacement of Hydrogen by the use of Halogen Compounds.**—The halogen compounds used are those of phosphorus, sulphur, antimony and iodine, and also sulphuryl chloride and bleaching powder. When phosphorus pentachloride is used the halogen does not enter the nucleus until the hydrogen of the side chain has been completely replaced. A mixture of red phosphorus and bromine is used in place of phosphorus bromide; with yellow phosphorus the reaction is much too vigorous. As red phosphorus generally contains traces of free phosphoric acid it should be previously washed with water or ammonia, and dried before using. Sulphur bromide and iodide are used in presence of nitric acid; with these the halogen enters the nucleus, and only mono-derivatives are formed. Antimony pentachloride yields two atoms of halogen for chlorination. Iodine monochloride in glacial acetic acid or dilute hydrochloric acid replaces hydrogen by iodine. Sulphuryl chloride chlorinates aromatic compounds, both in the side chain and in the nucleus; when a carbonyl or carboxyl group is present the hydrogen in the α-position to this group is substituted. Bleaching powder is used as a chlorinating agent owing to the ease with which it gives up its available chlorine.

PREPARATION 330.—**α-Bromostearic Acid** (*2-Bromo-octadecan acid*).

$$CH_3(CH_2)_{15}CHBrCOOH. \qquad C_{18}H_{35}O_2Br. \qquad 363.$$

30 gms. (3 mols.) of stearic acid and 1·1 gms. (1 atom) of red phosphorus are placed in a flask fitted with a reflux condenser and dropping funnel. The flask is immersed in a water bath containing water at 60°—70°, so that the stearic acid melts, and 22·5 gms. (4 mols.) of dry bromine are added gradually from the dropping funnel. When addition is complete the mixture is heated on a boiling water bath for about 3 hours. The product is poured into water, and the monobromostearic acid filtered off and dried on a porous plate. It is recrystallised from carbon disulphide.

$$3CH_3(CH_2)_{16}COOH + P + 4Br_2 = 3CH_3(CH_2)_{15}CHBrCOBr + HPO_3 + 2HBr.$$
$$CH_3(CH_2)_{15}CHBrCOBr + H_2O \rightarrow CH_3(CH_2)_{15}CHBrCOOH.$$

Colourless plates; M.P. 61°; the materials used in this preparation must be pure and dry (see next preparation). (B., 24, 2903; 25, 482.)

PREPARATION 331.—**Monobromoacetic Acid** [*Bromo-ethan Acid*].

$$CH_2BrCOOH. \qquad C_2H_3O_2Br. \qquad 139.$$

The materials for this preparation must be pure and dry. The acetic acid is purified, as on p. 241; the bromine is shaken with conc. sulphuric acid, and the phosphorus warmed with dilute ammonia, washed well with water, and dried in a steam oven.

20 gms. (3 mols.) of pure glacial acetic acid and 3 gms. (1 atom) of red phosphorus are placed in a round-bottomed flask of about 300 c.cs. capacity. (*N.B.*—Rubber stoppers should not be used.)

71 gms. (4 mols.) of bromine are added from a dropping funnel very gradually at first, the flask being cooled by immersion in cold water. The reaction proceeds with great vigour, but moderates after about half

of the bromine has been added, when the remainder may be run in more quickly. The flask is then warmed on a boiling water bath until the colour of bromine vapour in the interior of the flask disappears. After cooling, the bromo-acetyl bromide is poured into a distilling flask and distilled under diminished pressure.

The product is weighed, and the theoretical amount of water required to convert it into bromoacetic acid added gradually (1·8 gms. for 20 gms. of the acyl bromide). The mixture solidifies to a white crystalline mass. This is purified by distilling under ordinary pressure from a small distilling flask provided with an air condenser, the portion distilling at 190°—210° being retained.

$$3CH_3COOH + P + 8Br = 3CH_2BrCOBr + HPO_3 + 2HBr.$$
$$CH_2BrCOBr + H_2O \rightarrow CH_2BrCOOH.$$

*Yield.*—Variable. Colourless crystals; M.P. 50°—51°; B.P. 208°.

*Note.*—The bromoacetyl bromide and bromoacetic acid must not be allowed to touch the hands as they cause serious wounds.

(B., 20, 2026; A., 242, 141.)

PREPARATION 332.—**Monobromosuccinic Acid** [2-*Bromo-butan-diacid*].

$$COOH.CH_2.CHBrCOOH. \qquad C_4H_5O_4Br. \qquad 197.$$

A tubulated retort is sealed to a Liebig's condenser, and the latter connected to an apparatus to absorb hydrobromic acid. 18 gms. (3 mols.) of carefully dried succinic acid are intimately mixed with 3·5 gms. (excess) of red phosphorus. This is placed in the retort, and 80 gms. (excess) of bromine are added slowly from a dropping funnel through the tubulus. The bromine must be very carefully added at the beginning as the reaction is violent, and again added only when the reaction subsides. When all the bromide has been added, the whole is heated on a water bath until the bromine disappears. The retort now contains monobromosuccinyl bromide; the free acid is obtained by pouring *slowly* the contents of the retort into 100 c.cs. of boiling water, the flame being withdrawn. It is then filtered, and repeatedly extracted with ether, the latter removed on the water bath, and the residue recrystallised from water.

$$3\begin{array}{l}CH_2.COOH\\ |\\ CH_2.COOH\end{array} + 2P + 8Br_2 \rightarrow 3\begin{array}{l}CH.Br.COBr\\ |\\ CH_2.COBr\end{array} + 2HPO_3 + 7HBr.$$

$$\begin{array}{l}CHBr.COBr\\ |\\ CH_2COBr\end{array} + 2H_2O \rightarrow \begin{array}{l}CH.Br.COOH\\ |\\ CH_2COOH.\end{array}$$

*Yield.*—85% theoretical (25 gms.). Colourless crystals; M.P. 160°; soluble in water. (A., 242, 145; B., 14, 892.)

PREPARATION 333.—**2 : 4 : 1-Iodonitroaniline** (1-*Amino*-2-*iodo*-4-*nitro-benzene*).

$$C_6H_3(NH_2)(NO_2)I. \qquad C_6H_5O_2N_2.I. \qquad 264.$$

15 gms. (1 mol.) of finely ground *p*-nitroaniline are agitated with cold glacial acetic acid in quantity just sufficient to bring all into solution. A solution of 26·5 gms. (1 mol.) of iodine monochloride in glacial acetic

acid is then slowly added to the well-stirred solution, which after the addition is allowed to stand 1 hour. It is then poured into 1·5 litres of boiling water, filtered and allowed to cool. After some time crystals of iodonitroaniline separate which are filtered off and dried.

$$C_6H_4(NH_2)(NO_2) + ICl \rightarrow C_6H_3(NH_2)(NO_2)I + HCl.$$

Long yellow needles; soluble in hot water; M.P. 105°. (B., 34, 3344.)

PREPARATION 334.—**Monochloromalonic Acid** [*2-Chloro-propan-diacid*].

$CH.Cl(COOH)_2$. $C_3H_3O_4Cl$. 138·5.

8 gms. (1 mol.) of malonic acid from a sample which has been dried in a steam oven and cooled in a desiccator are dissolved in 250 c.cs. of anhydrous ether. The solution is cooled in ice-water, and 10 gms. (1 mol.) of sulphuryl chloride slowly added. The ether is removed on a water bath, and the residue left in a vacuum desiccator containing sulphuric acid until crystallisation of mono-chloromalonic acid is complete.

$$CH_2(COOH)_2 + SO_2Cl_2 \rightarrow CHCl(COOH)_2 + HCl + SO_2.$$

*Yield.*—Theoretical (10·5 gms.). Colourless crystals; M.P. 133°. (B., 35, 1814.)

**Reaction CLXVI. Replacement of the Amino Group by Halogen.**—The amino group can easily be replaced by halogen :—

(*a*) By means of the Sandmeyer reaction. The amine is diazotised and the resulting diazonium solution added to a warm solution of cuprous halide.

$$R.NH_2 \rightarrow R.N_2Cl \rightarrow R.Cl + N_2.$$

(*b*) By Gattermann's method, in which copper powder is added to an acid solution of the diazonium salt.

(*c*) By heating a solution of the diazonium compound with hydriodic acid or potassium iodide.

PREPARATION 335.—***o*-Bromotoluene.**

$C_6H_4(CH_3).Br$. $C_7H_7Br$. 171.

6 gms. *ortho*-toluidine are dissolved in a mixture of 35 c.cs. hydrobromic acid of constant boiling pont, and 40 c.cs. of water. The solution is cooled to 0°, and diazotised by the addition of 5 gms. sodium nitrite dissolved in 12 c.cs. of water; during this addition a drop is frequently removed, diluted with water on a watch-glass, and tested with starch-iodide paper for free nitrous acid (see p. 373). Copper powder (prepared from 40 gms. copper sulphate, see p. 508) is then added in small quantities at a time to the diazonium solution, which should be continuously stirred; an effervescence—due to the escape of nitrogen—takes place. When addition of copper produces no further effervescence, the bromo-toluene forms the lower layer. This layer is separated, steam distilled and the distillate extracted with ether. The ethereal solution is dried over solid calcium chloride, and fractionated.

$$CH_3.C_6H_4.NH_2 \rightarrow CH_3.C_6H_4N_2Br \rightarrow CH_3.C_6H_4.Br.$$

*Yield.*—70% theoretical (6 gms.). B.P. 181°. (G., 29, 631; O. S., IX., 22).

PREPARATION 336.—***p*-Chlorotoluene** (1-*methyl*-4-*chlorobenzene*).

$CH_3.C_6H_4.Cl.$ $C_7H_7Cl.$ 126·5.

20 gms. (1 mol.) of *p*-toluidine are dissolved in 100 c.cs. of a mixture of equal volumes of water and conc. hydrochloric acid, and diazotised in the usual way (see p. 372) with sodium nitrite. 15 gms. of moist copper powder (see p. 508) are then added in small portions to the well-stirred solution. When the evolution of nitrogen has ceased, the product is steam distilled, the distillate extracted with ether, and the ethereal solution dried over anhydrous sodium sulphate. The sodium sulphate is filtered off and the filtrate distilled. *p*-Chorotoluene passes over at 163°.

$$CH_3.C_6H_4.NH_2 \rightarrow CH_3.C_6H_4N_2Cl \rightarrow CH_3.C_6H_4Cl + N_2.$$

*Yield.*—70% theoretical (17 gms.). Colourless oily liquid ; M.P. 7·4° ; B.P. 163°. (B., 23, 1218 ; O. S., III., 33.)

PREPARATION 337.—**Chlorobenzene.**

$C_6H_5.Cl.$ 112·5.

20 gms. aniline are dissolved in 130 c.cs. water and 37 c.cs. conc. hydrochloric acid, and diazotised (see Preparation 379) at 0°—5° by the addition of 15 gms. sodium nitrite dissolved in 40 c.cs. water. 140 c.cs. of a 10% solution of cuprous chloride (p. 507) are heated nearly to boiling in a flask and the diazonium solution run in gradually, the contents of the flask being occasionally shaken, and maintained near boiling during the addition.

The yellow precipitate which appears on the introduction of the diazonium solution decomposes almost immediately, yielding chlorobenzene and nitrogen. The contents of the flask are submitted to steam distillation until no more oily drops of chlorobenzene pass over. The distillate is extracted with ether, the ethereal solution dried over calcium chloride and fractionated.

$$C_6H_5N_2Cl \rightarrow C_6H_5.Cl + N_2.$$

*Yield.*—75% theoretical (18 gms.). Colourless liquid ; B.P. 132°. (B., 23, 1628, 1880 ; A., 272, 141.)

PREPARATION 338.—***p*-Iodotoluene.**

$CH_3.C_6H_4.I.$ $C_7H_7I.$ 218.

20 gms. *p*-toluidine are boiled with 70 c.cs. conc. hydrochloric acid and sufficient water to dissolve the hydrochloride. The solution is diazotised as usual (p. 372), and 31 gms. potassium iodide dissolved in water are then run in from a tap funnel with continuous stirring. The mixture is allowed to stand for a time when a dark brown mass is formed which is filtered off and recrystallised from alcohol.

$$CH_3C_6H_4NH_2 \rightarrow CH_3C_6H_4N_2Cl \rightarrow CH_3C_6H_4I.$$

*Yield.*—80% theoretical (25 gms.). Yellow plates ; M.P. 35° ; B.P. 211°.

**Reaction CLXVII. Replacement of Halogen by Halogen.**—The substitution of bromine by chlorine can be effected through the use of the

pentachlorides of antimony or phosphorus. Iodine is still more readily replaced by chlorine, not only by direct action of the latter, but also by double decomposition with certain metallic chlorides ($HgCl_2$, $SbCl_5$, AgCl) or iodine trichloride.

The substitution of chlorine by the direct action of bromine is rarely effected. Aluminium bromide, cupric bromide in alcoholic solution or boron tribromide under pressure, convert many alkyl chlorides into alkyl bromides. Mono-chloroacetic acid heated to 150° in a sealed tube with hydrobromic acid or potassium bromide yields mono-bromoacetic acid.

Iodine may be replaced by bromine by direct action or by heating under pressure with bromides of copper, mercury, silver or boron.

Bromine and chlorine can be replaced by iodine through double decomposition with hydriodic acid or iodides of potassium, calcium or aluminium.

Aliphatic fluoro-compounds may be prepared from $SbF_3$ and chloro-compounds, or from olefines and HF. (Am. Soc., 56, 1195, 1782.)

PREPARATION 339.—**Iodoacetic Acid.**

$CH_2I.COOH$. $C_2H_3O_2I$. 186.

25 gms. (1 mol.) of chloroacetic acid dissolved in 125 c.cs. of absolute alcohol and 50 gms. (excess) of finely powdered potassium iodide are refluxed on a water bath for 1 hour. The product is well cooled in ice-water, and filtered from potassium chloride and iodide. The filtrate is decolorised (if necessary), by passing in a stream of sulphur dioxide, and afterwards evaporated to a small bulk on a water bath. On cooling, a product separates which is collected, dried by exposure in air, and re-crystallised from a large volume of petroleum ether.

Colourless leaflets ; M.P. 84° ; the solid causes painful blisters in contact with the skin, and the vapours irritate the eyes. (B., 41, 2853.)

PREPARATION 340.—**Glyceryl Tribromide** [1 : 2 : 3-*Tribromo-propan*].

$CH_2.Br.CHBr.CH_2Br$. $C_3H_5Br_3$. 281.

75 gms. (slight excess) of bromine are slowly added to 50 gms. (1 mol.) of allyl iodide contained in a flask, fitted with an air condenser, and well cooled in a freezing mixture ; the whole apparatus being set up in a fume cupboard. The liquid is allowed to stand 24 hours, and filtered from the iodine which has crystallised out. The brown filtrate is repeatedly washed with dilute caustic soda, with sodium thiosulphate solution, and with water ; it is then dried over fused calcium chloride and distilled. The distillate is again treated with sodium thiosulphate solution and with water, dried and distilled. The fraction 200°—220° is allowed to stand in a freezing mixture, and the mother liquor is then poured off from the crystals which form. The product is purified by repeated distillations.

Colourless glistening prisms ; insoluble in water ; M.P. 16° ; B.P. 219°—220°. (A. Ch., [3], 48, 304 ; [3], 51, 91 ; C. r., 70, 638 ; A., 156, 168.)

**Reaction CLXVIII. Replacement of Hydrogen by Molecular Halogen.**—Chloro- and bromo-derivatives of the aliphatic hydrocarbons are obtained by the action of chlorine and bromine on these hydrocarbons in presence

of light, the reaction being more energetic in sunlight than in diffused light. The corresponding iodo-derivatives cannot be obtained in this way, due, it is supposed, to the energetic reducing action of hydriodic acid, which converts the iodo-derivative into the original paraffin. Iodination of aromatic hydrocarbons, however, takes place in presence of oxidising agents (*e.g.* nitric acid) (O.S., IX, 46).

In the case of aromatic bodies the temperature has an important influence on the part of the molecules the chlorine or bromine will attack; in the cold in the presence of carriers, the halogen enters the nucleus, while at the boiling point the side chain is attacked. The carriers most frequently used are: iron, aluminium-mercury couple, iodine, halides of phosphorus, antimony, iron, aluminium, sulphur or pyridine. The halogen is always more active in sunlight, or in ultra-violet light.

The presence of hydroxyl-, amino- or substituted amino-groups in the aromatic nucleus facilitates halogenation (*cf.* Preps. 352 and 353).

A solvent is frequently employed, either to dissolve the compound or to moderate the action of the halogen; those commonly employed are carbon tetrachloride, glacial acetic acid, carbon disulphide, ethylene dichloride, chloroform, ether, water, hydrochloric acid, sulphuric acid. It is not always a matter of indifference which solvent is selected.

In some cases the operation has to be conducted in a sealed tube under pressure, and if a solvent is also employed carbon tetrachloride is generally the most suitable. For direct halogenation under pressure, see Ann. Chim. App., 1935, 163.

PREPARATION 341.—**Dibromosulphanilic Acid** (2 : 6-*Dibromo*-1-*amino*-4-*benzenesulphonic acid*).

$$C_6H_2Br_2(NH_2)(SO_3H). \qquad C_6H_5O_3NBr_2S. \qquad 331.$$

10 gms. (1 mol.) of sulphanilic acid are dissolved in about 1 litre of warm water. The solution, when cold, is placed in a large bottle or flask which is connected to a suction pump on one side, and to a wash-bottle containing 18·5 gms. (2 mols.) bromine on the other. In this way a stream of air laden with bromine vapour is drawn through the solution. When the bromine has completely disappeared, the liquid is filtered, and concentrated on a water bath until a sample yields a large crop of crystals on cooling. The whole is allowed to cool, the crystals separated and dried. The mother liquor may yield a second crop after further concentration.

$$C_6H_4(NH_2)(SO_3H) + 2Br_2 \rightarrow C_6H_2Br_2(NH_2)(SO_3H) + 2HBr.$$

*Yield*.—90% theoretical (16 gms.). Colourless needles; soluble in hot water; decomposes at 180°. (A., 120, 138.) For the conversion of sulphanilic acid into tribromoaniline by nascent bromine, see p. 501.

PREPARATION 342.—**Chlorobenzene** (*Phenylchloride*).

$$C_6H_5Cl. \qquad 112{\cdot}5.$$

For suitable apparatus, see Fig. 49.

100 gms. of pure, dry benzene are heated to boiling with 1 gm. wrought

iron powder in a large round-bottomed flask with reflux condenser attached. A stream of dry chlorine is passed through at a temperature of 79° with vigorous stirring. It is essential that the chlorine should be dried, and at least three wash-bottles of conc. sulphuric acid and a calcium chloride tube are recommended. The hydrochloric acid evolved during the reaction may be absorbed in a flask which contains a layer of water. Chlorine is passed in until about 90% of the calculated quantity is used up. The chlorination lasts about 5 hours, and the weight should be increased by 43 gms. The gas should be well regulated, otherwise unchanged benzene will be carried off. If the chlorine inlet tube becomes stopped up with dichlorobenzene, the stream of gas should be interrupted for a time when the solid will dissolve again. The chlorination mixture is allowed to stand, and is poured off from the iron sludge. The mixture is rectified by means of a fractionating column. The fraction 126°—133° is redistilled through the column, and the fraction 131°—132° collected.

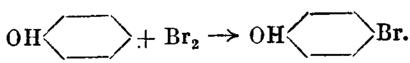
$$C_6H_6 + Cl_2 \longrightarrow C_6H_5Cl + HCl.$$

*Yield.*—90% theoretical (130 gms.). Colourless liquid; B.P. 132°; D. $^{0}_{4}$ 1·1284. (B., 11, 117; 26, 1053.).

PREPARATION 343.—*p*-**Bromophenol.**


$C_6H_5OBr$. 173.

100 c.cs. of carbon disulphide and 100 gms. of phenol are placed in a round-bottomed flask fitted with a mechanical agitator, and to which is attached a reflux condenser and a dropping funnel through a rubber stopper. 170 gms. of bromine (54·6 c.cs.) dissolved in 50 c.cs. of carbon disulphide are placed in the dropping funnel. The flask is cooled to 0°—5° in a freezing mixture, and after starting the agitation the bromine is slowly run in, the addition requiring about 2 hours. The mixture is distilled to remove the carbon disulphide. The residue is distilled *in vacuo*, using a Claisen flask and a good fractionating column. The fraction 145°—150° at 25—30 mms. is collected, and on cooling sets to a solid white mass, which may be dried by pressing on a porous plate.



*Yield.*—80—84% theoretical (145—155 gms.). M.P. 63°—64°.

*Note.*—The *p*-bromophenol should not be allowed to come in contact with the stopper.

(A., 137, 200; B., 1176; O. S., I., 39.)

PREPARATION 344.—**Benzyl Chloride** [*Phenyl-chloro-methan*].

$C_6H_5.CH_2.Cl$. $C_7H_7Cl$. 126·5.

50 gms. toluene are placed in a tared retort (Fig. 49 or 55), the neck of which is sloped upwards and connected to a water reflux condenser carrying a straight calcium chloride tube at the end. 2 gms. phosphorus pentachloride or phosphorus trichloride to act as chlorine carrier are also placed in the retort. The toluene is boiled and a stream of dry chlorine is

led through the liquid by a delivery tube fixed by a cork (an ordinary cork, previously soaked in melted paraffin wax should be used) in the neck of the retort. The retort is weighed periodically, and the stream of chlorine continued until an increase in weight of 18·5 gms. takes place. The product is distilled, the fraction 165°—185° being collected; this is

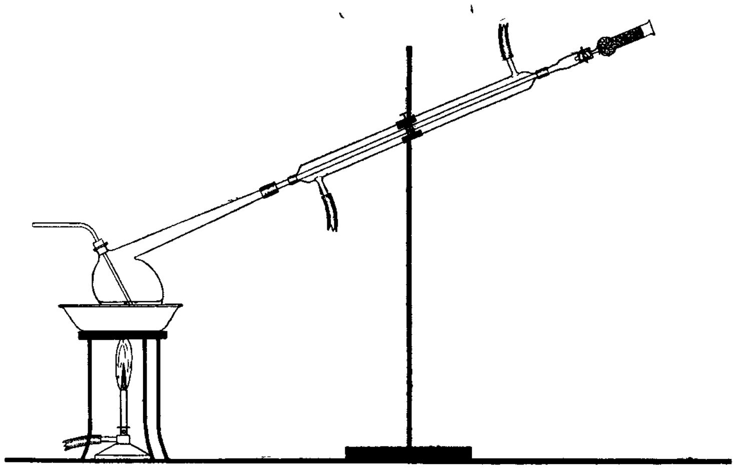


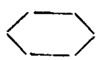
FIG. 55.

redistilled, collecting the fraction 176°—180°, which is practically pure benzyl chloride.

$$C_6H_5.CH_3 + Cl_2 \rightarrow C_6H_5CH_2Cl + HCl.$$

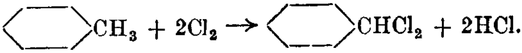
*Yield.*—60% theoretical (40 gms.). B.P. 176°; D.$^{15}_{15}$ 1·04. (A., 1853 88, 129; B., 18, 606; A., 272, 149.) See also J. C. S., 1936, 337.

PREPARATION 345.—**Benzylidene Chloride** (*Benzal chloride*).

 $CHCl_2$.  $C_7H_6Cl_2$.  161.

445 gms. toluene and 10 gms. phosphorus pentachloride are heated to boiling in a litre flask provided with a reflux and agitator (Fig. 49). Dry chlorine is passed into the liquid until the increase in weight is 355 gms. The chlorination is facilitated by bright sunlight, or by ultra-violet light. The chlorination mixture is then fractionally distilled and the fraction between 160°—225° collected. The latter is further fractionated, and the portion between 200°—210° collected and purified by distillation.

The impurities present after chlorination are unchanged toluene, benzyl chloride and benzotrichloride.




*Yield.*—85% theoretical (660 gms.). Colourless liquid; B.P. 212°; D. 1·2557. (A., 116, 336; 146, 322; 139, 318.)

PREPARATION 346.—*p*-**Nitrobenzyl Bromide.**

$$NO_2.C_6H_4.CH_2Br. \qquad C_7H_6O_2NBr. \qquad 216.$$

*Method I.*—5 gms. pure *p*-nitrotoluene, 2 c.cs. of bromine, and a crystal of iodine are placed in a sealed tube. The tube is placed in a bomb furnace and gradually heated up during 40 minutes to 130°, at which temperature it is maintained for 160 minutes. After cooling, the tube is opened and the product extracted with about 60 c.cs. of hot alcohol. From the resulting solution crystals separate on cooling, which are filtered off; a second crop is obtained after concentrating and cooling the mother liquor. Water is added to the final mother liquor to precipitate a small quantity of the nitrobenzyl bromide, which is filtered off, dried, and purified by recrystallisation from petroleum ether. The first and second crops should be washed with cold petroleum ether.

*Yield.*—75% theoretical (6 gms.).

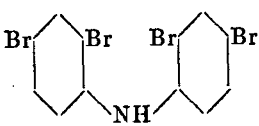
*Method II.*—10 gms. of *p*-nitrotoluene and a crystal of iodine dissolved in 100 c.cs. of carbon tetrachloride are placed in a silica flask provided with a reflux condenser. The solution is covered with water (about 50 c.cs.) and heated to gentle boiling, while situated about 15 cms. from a mercury vapour lamp (Fig. 46). A solution of 15 gms. bromine in 50 c.cs. carbon tetrachloride is then run in drop by drop from a dropping funnel at the top of the condenser. When all the bromine is in, boiling is continued until the solution becomes almost colourless. The contents of the flask are cooled, transferred to a separating funnel, and the lower carbon tetrachloride layer run into a distilling flask. Carbon tetrachloride is distilled off over a water bath, and the residue of *p*-nitrobenzyl bromide recrystallised from alcohol or petroleum ether.

$$NO_2.C_6H_4CH_3 + Br_2 \rightarrow NO_2C_6H_4CH_2Br + HBr.$$

*Yield.*—80% theoretical (12·6 gms.). Needles; M.P. 99°—100°. (See also Am. Soc., 40, 406; J. R. T. C., I., 58.) A useful reagent for the identification of phenols and acids.

It is worthy of note that *o*-nitrotoluene is not brominated by this method even at temperatures up to 200°—an interesting example of "steric hindrance." The *m*-compound, on the other hand, gives a 20% yield of the bromo-compound.

PREPARATION 347.—**Tetrabromodiphenylamine** (2 : 4 : 2′ : 4′-*Tetrabromo*-1 : 1′-*diphenylamine*).



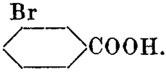

$C_{12}H_7NBr_4$. 485.

4 gms. (1 mol.) of finely powdered diphenylamine are agitated with a sufficient quantity of cold glacial acetic acid to dissolve. The solution is stirred while 5 c.cs. (4 mols.) of bromine dissolved in 50 c.cs. glacial acetic acid are slowly run in. The tetrabromodiphenylamine formed separates as a precipitate, which is filtered off and recrystallised from alcohol.

$$(C_6H_5)_2NH + 4Br_2 \rightarrow (C_6H_3Br_2)_2NH + 4HBr.$$

*Yield.*—Theoretical (12 gms.). Colourless needles; M.P. 182°. (A., 132, 166; B., 8, 825.)

PREPARATION 348.—*m*-**Bromobenzoic Acid** (1-*Carboxy*-3-*bromobenzene*).



$C_7H_5O_2Br$. 201.

6 gms. (1 mol.) of benzoic acid, 8 gms. (1 mol.) of bromine, and 40 gms. of water are heated together in a thick-walled sealed tube to about 140°—150° in the usual type of furnace for 9 hours. After cooling, the tube is opened with the usual precautions, and the colourless crystals of bromobenzoic acid washed out, filtered, and boiled with 100 c.cs. of water in a basin for 1 hour to remove unchanged benzoic acid. The residual bromobenzoic acid is then recrystallised twice from hot water.

$$C_6H_5.COOH + Br_2 = C_6H_4(Br)CO.OH + HBr.$$

*Yield.*—80% theoretical (8 gms.). Colourless needles; soluble in hot water; M.P. 155°. (A., 149, 131.)

PREPARATION 349.—**Dibromosuccinic Acid** [2 : 3-*Dibromo-butan-diacid*].

$$\begin{array}{l} CHBrCOOH \\ | \\ CHBrCOOH \end{array} \qquad C_4H_4O_4Br_2. \qquad 276.$$

12 gms. (1 mol.) of succinic acid, 32 gms. (1 mol.) of bromine, and 12 gms. of water are heated in a sealed tube for 6 hours at 170° (see p. 41). The tube is then opened in the usual way. The greyish-white mass with which the tube is now filled is recrystallised from boiling water, with the addition of a little animal charcoal.

$$\begin{array}{l} CH_2.COOH \\ | \\ CH_2.COOH \end{array} + 2Br_2 = \begin{array}{l} CHBrCOOH \\ | \\ CHBrCOOH \end{array} + 2HBr.$$

*Yield.*—Theoretical (27 gms.). Colourless glistening crystals; soluble in hot water, in alcohol and in ether; decomposes at 200° with formation of hydrobromic acid and bromo-maleic acid. (A., 117, 120; A. Spl., 1, 351; Bl., 18, 168.)

PREPARATION 350.—α-**Bromonaphthalene.**

$C_{10}H_7Br$. 207.

116 gms. of naphthalene (flakes) and 125 c.cs. of water are placed in a pot fitted with a good mechanical agitator and heated to 40°—50°. 145 gms. (45 c.cs.) of bromine are then gradually dropped in from a dropping-funnel dipping to the bottom of the pot at such a rate that the temperature is maintained at 40°—50°. The addition takes 8—9 hours. After all the bromine has been added, stirring is continued until the colour has practically disappeared. The mixture is allowed to cool, and a heavy oil separates. The oil is steam distilled on an oil bath at 145°—

150°, this process removing the hydrobromic acid and some unchanged naphthalene. The oil is distilled *in vacuo*, the fraction 132°—133° 12 mms. (145°—148° at 20 mms.) being collected. The lower fractions contain naphthalene, and the higher, 1 : 4-dibromonaphthalene.

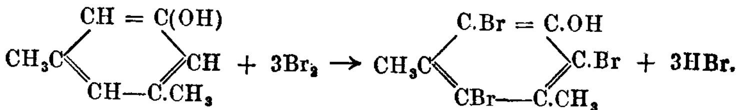
$$C_{10}H_8 + Br_2 = C_{10}H_7Br + HBr.$$

*Yield.*—55—60% theoretical (100—110 gms.). B.P. 281°; M.P. 4°. (A., 135, 40; 147, 166; O. S., I., 35; X., 14.)

PREPARATION 351.—**Tribromo-*s*-xylenol.**

$(CH_3)_2C_6Br_3(OH)$. $C_8H_7OBr_3$. 359.

A few gms. of *s*-xylenol are placed in a large test tube or small beaker, and covered with about 20 times their weight of water. Bromine is gradually added drop by drop until an excess is indicated by a reddish-brown colour which does not disappear. Sulphur dioxide, either as aqueous solution or gas, is added until the excess of bromine is removed. The precipitate is filtered off, washed with water, and recrystallised from alcohol.



*Yield.*—90% theoretical. Fine needles; M.P. 166°. (B., 18, 2679; A., 281, 122.)

PREPARATION 352.—**Tribromophenol** (1 - *Hydroxy* - 2 : 4 : 6 - *tribromo - benzene*).

$C_6H_2(OH)Br_3$. $C_6H_3OBr_3$. 331.

5 gms. (1 mol.) of phenol are dissolved in 100 c.cs. of water, and to the cold solution 8·3 c.cs. (3 mols.) of bromine in aqueous solution are added. The precipitate, which is almost insoluble in water, is filtered off, washed with water, and recrystallised from dilute alcohol.

$$C_6H_5(OH) + 3Br_2 \rightarrow C_6H_2Br_3(OH) + 3HBr.$$

*Yield.*—Theoretical (17 gms.). Colourless needles; M.P. 95°. (A., 43, 212; 137, 208.) For estimation of phenol by bromination, see p. 501.

PREPARATION 353.—***p*-Bromodimethylaniline.**

$C_6H_4BrN(CH_3)_2$. $C_8H_{10}NBr$. 200.

10 gms. dimethylaniline are dissolved in glacial acetic acid, and 6·6 gms. bromine dissolved in glacial acetic acid gradually added. When the solution is diluted with water, the *p*-bromo-dimethylaniline is precipitated, filtered off, and recrystallised from alcohol.

$$C_6H_5N(CH_3)_2 \rightarrow C_6H_4Br.N(CH_3)_2.$$

*Yield.*—Almost theoretical (16—17 gms.). White plates; M.P. 55°. (B., 8, 715.)

PREPARATION 354.—**Benzoyl Chloride.**

$C_6H_5COCl$. $C_7H_5OCl$. 140·5.

Dry chlorine is led into cold benzaldehyde (for apparatus, see p. 63). The chlorine is easily absorbed with evolution of heat, torrents of hydro-

chloric acid being given off. When the reaction has moderated somewhat, heat is applied in order to keep the liquid boiling briskly, the stream of chlorine being continued until the evolution of hydrochloric acid ceases. The excess chlorine is removed by passing a stream of dry air or carbon dioxide through the apparatus. The product is then distilled.

$$C_6H_5C\begin{matrix}\nearrow O\\ \searrow H\end{matrix} \rightarrow C_6H_5C\begin{matrix}\nearrow O\\ \searrow Cl.\end{matrix}$$

*Yield.*—Almost theoretical. Colourless, fuming liquid, with irritating smell; B.P. 198°; D. $^{19}_{19}$ 1·214. (A., 3, 262.)

PREPARATION 355.—**Chloral** (*Trichloroacetaldehyde*).

$$CCl_3CHO. \qquad C_2HOCl_3. \qquad 147{\cdot}5.$$

100 c.cs. absolute alcohol are placed in a retort, with the side tube on the slant, and attached to a reflux. A current of dry chlorine is passed into the alcohol, the temperature being kept at 5°—10° by external cooling. The gas is quickly absorbed at first, but the absorption slackens off. The contents of the retort are heated to 60°, while chlorine is still passed, as long as it is absorbed. The liquid is then boiled gently and cooled—its specific gravity should now be 1·400. An equal volume of conc. sulphuric acid is then cautiously added, ethyl chloride and hydrochloric acid being evolved. The mixture is distilled from a water bath. The distillate is neutralised with chalk and again distilled, and finally fractionated, the fraction boiling at 95°—100° being retained.

$$CH_3CH_2OH \xrightarrow{Cl} CH_3CHO \xrightarrow{Cl} CCl_3CHO \rightarrow CCl_3CH(OH)OC_2H_5 \rightarrow CCl_3CHO.$$

Colourless liquid; characteristic odour; B.P. 98°. (Z. Ch., 1870, 172; A., 279, 293.)

When chloral is mixed with $\frac{1}{5}$ its weight of water, the mixture gradually solidifies to a crystalline mass of chloral hydrate.

$$CCl_3CHO + H_2O \rightarrow CCl_3CH(OH)_2.$$

Colourless crystals; M.P. 57°; B.P. 97°, with decomposition; is converted into chloral by sulphuric acid. (Z., 1870, 172, 351.)

PREPARATION 356.—**Monochloroacetic Acid.**

$$CH_2Cl.COOH. \qquad C_2H_3O_2Cl. \qquad 94{\cdot}5.$$

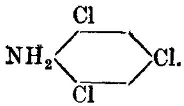
100 gms. glacial acetic acid and 10 gms. of sulphur are placed in a small flask, and the whole weighed. The flask is fitted with a two-holed cork, one hole being fitted with an adapter, to which is attached a reflux condenser, while the other is fitted with a delivery tube reaching down into the acid. The flask is heated on a boiling water bath, and a steady current of chlorine passed into the acid until (about 6 hours) a gain in weight of 50 gms. has taken place. It is important to place the apparatus in direct sunlight as this has a catalytic accelerating effect on the operation. When the required increase has taken place, the liquid is decanted from the sulphur into a distilling flask and distilled through an air condenser. Acetyl chloride, sulphur chloride and acetic acid come

over at first. The fraction 150°—190° is collected separately; this yields crystals of mono-chloroacetic acid, on cooling; the liquid is drained off from the crystals, the latter redistilled, and the fraction 180°—190° collected.

$$CH_3.COOH + Cl_2 \rightarrow CH_2Cl.COOH + HCl.$$

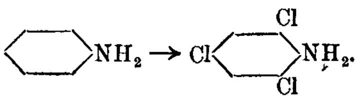
*Yield.*—45—60% theoretical (75—100 gms.). Colourless crystals. M.P. 62°—63°; B.P. 185°—187°. (Bl., [3], 2, 145; Z. a., 40, 973.)

PREPARATION 357.—**Trichloroaniline** (1-*Amino*-2 : 4 : 6-*trichlorobenzene*).



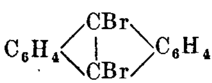
$C_6H_4NCl_3$. 196·5.

10 gms. of dry aniline are dissolved in 200 gms. dry carbon tetrachloride, and placed in a flask fitted with a mechanical agitator (see Fig. 49). The flask is surrounded by an efficient freezing mixture, so that the temperature is about − 10°. Through one of the side tubes is passed dry chlorine mixed with dry carbon dioxide (equal volumes). A white crystalline deposit of trichloroaniline is thrown down, but if the temperature is allowed to rise or the materials are not absolutely dry, the product is contaminated with aniline black. The crystals are filtered off and recrystallised from alcohol.



*Yield.*—Almost theoretical (21 gms.). White needles; M.P. 77·5°; B.P. 262°. (J. S. C. I., 45, 355.)

PREPARATION 358.—**9 : 10-Dibromoanthracene.**



$C_{14}H_8Br_2$. 336.

50 gms. of anthracene (80—85%) and 500 c.cs. of carbon tetrachloride are placed in a flask with mechanical agitator and reflux condenser affixed. 95 gms. of bromine are slowly added with vigorous agitation, and the dibromo compound separates. The hydrogen bromide evolved is led from the top of the condenser to a fume duct or is absorbed in water. The addition of bromine takes about 30 minutes. The mixture is then gently raised to boiling and maintained there for 1 hour. It is cooled, allowed to stand for some hours, and the dibromo compound filtered off, washed with carbon tetrachloride, and dried. A further yield is obtained by concentrating the mother liquor. The product is crystallised from carbon tetrachloride or from toluene.

$$C_{14}H_{10} + 2Br_2 \rightarrow C_{14}H_8Br_2 + 2HBr.$$

*Yield.*—85% theoretical (70 gms.). Yellow needles; M.P. 217°. (O. S., III., 41.)

## CHAPTER XXIII

### THE LINKING OF HYDROGEN TO NITROGEN

### Amino Compounds

**Reaction CLXIX. Action of Metals on Nitro Compounds in Acid Media.** —Primary amines are formed.

$$R.NO_2 + 3M'' + 6HCl \longrightarrow R.NH_2 + 3M''.Cl_2 + 2H_2O.$$

The metals used are iron, zinc, tin; and the acids, hydrochloric, sulphuric, and in some cases acetic. As a rule, the best temperature for the reduction is about 100°, and in some cases the nitro compound may be dissolved in a suitable solvent. In all cases, good mechanical agitation is essential to prevent the metal settling to the bottom of the pot.

The amine is obtained in the form of its salt, the base being liberated by caustic soda. The amine, if volatile in steam, is separated by steam distillation; solid amines are separated by filtration. Sometimes the amine may be extracted with ether, but before this is done the metal should first be removed.

Where zinc and tin are used, double salts of the general formula, $R.NH_2.HCl.MCl_2$, sometimes separate out when the reduction is complete. These salts may be decomposed by excess of caustic soda, and the base isolated as before.

When iron is used along with hydrochloric acid, the acid acts as a catalyst, and very little need be used in the reaction (see note under aniline). Further, steam distillation can be effected without the addition of alkali.

PREPARATION 359.—**Aniline** (*Aminobenzene*).

$$C_6H_5NH_2. \qquad C_6H_7N. \qquad 93.$$

This compound should be made in a pot, as shown in Fig. 37, to which is attached a reflux condenser. The metal used in this reduction is iron, and should be in as fine a state as possible. The agitation should be very efficient.

60 c.cs. of water and 120 gms. of iron powder are placed in the reduction pot, agitation being maintained during the addition. The pot is then heated to 90°—95°, and 10 c.cs. conc. hydrochloric acid (D. 1·8) are poured in; 100 gms. nitrobenzene are then added, a few c.cs. at a time. The temperature must be held at 100°, and this can be conveniently done by regulating the addition of the nitrobenzene. When all the latter has been added, the reduction is continued at about 100° until no smell of nitrobenzene remains, or until a sample dissolves completely in dilute hydrochloric acid.

If the agitation is not powerful enough to carry through this process,

the following may be adopted: 100 gms. of nitrobenzene and 60 c.cs. water and 10 c.cs. of conc. hydrochloric acid (D. 1·18) are heated in the pot up to 95°. 120 gms. iron powder are then added carefully, the temperature being maintained at about 100°. After all the iron has been added, the temperature is maintained at 100° by external heat, and agitation continued until all the nitrobenzene has been reduced.

*Steam Distillation.*—If direct steam can be led into the reduction pot, this process is simplified, for, by merely altering the condenser to the usual sloping position, the aniline can be distilled off. If direct steam cannot be led into the reduction pot, the contents, after the reduction is finished, are poured into a large round-bottomed flask, and steam from a steam generator led into it, the products of vaporisation being condensed in the usual way (see Fig. 14).

*Separation.*—The condensate is poured into a separating funnel and allowed to stand until separation into two layers is complete. This may be assisted by applying heat or by adding salt. The aniline is then poured off, dried over solid caustic soda and distilled.

$$C_6H_5NO_2 + 3Fe + 6HCl \rightarrow C_6H_5NH_2 + 3FeCl_2 + 2H_2O.$$

*Yield.*—95% theoretical (70 gms.). B.P. 184°; D. 1·026; important intermediate for dyestuffs.

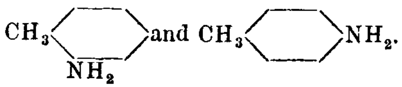
*Note.*—The quantity of hydrochloric acid used in an acid reduction where iron is employed is only about $\frac{1}{40}$ of the quantity required by theory.

Several theories have been advanced to explain this reaction. Ferrous chloride is formed at the outset, according to equation (1), while ferric hydroxide appears early in the reduction. At the end of the reduction the iron is almost completely in the form of $Fe_3O_4$. These two reactions may be explained by equations (2) and (3), and it is probable that the ferrous chloride catalyses both.

$$\begin{array}{ll} (1) & Fe + 2HCl \rightarrow FeCl_2 + H_2. \\ (2) & R.NO_2 + 2Fe + 4H_2O \rightarrow R.NH_2 + 2Fe(OH)_3. \\ (3) & 4R.NO_2 + 9Fe + 4H_2O \rightarrow 4R.NH_2 + 3Fe_3O_4. \end{array}$$

(A., 55, 200; B., 19, 903; 13, 1298; 19, 2916.)

PREPARATION 360.—*o*- **and *p*-Toluidines** (1 : 2- *and* 1 : 4-*Methyl-amino benzenes*).



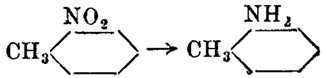

$C_7H_9N$. 107.

The reduction of nitrotoluene is similar to that given for nitrobenzene under aniline (p. 356). The steam distillation is similar, the *ortho*- and *para*-compounds formed in the reduction passing over.

*Separation of o- and p-Toluidine (a).*—The oil is separated from the water, ice and salt added, and the mixture stirred. A whitish-yellow crystalline compound will appear, which is the hydrate of the *p*-compound. This is filtered through an ice filter (Fig. 4), and the hydrate well pressed

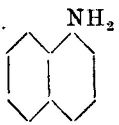
to remove any adhering oily *o*-compound. The *ortho*-compound passes through the filter along with the water, and is separated. The *para*-compound is recrystallised from alcohol. (J. S. C. I., 27, 258.) For separation by means of $SO_2$, see E.P., 355018.

*Separation of Pure o-Toluidine* (*b*).—The mixture of the *o*- and *p*-compounds is treated with conc. hydrochloric acid until slightly acid to Congo red, and water added until the solution is saturated at ordinary temperature. Saturated aqueous sodium ferrocyanide is then gradually added with shaking, when the greenish-white needles of *o*-toluidine hydro-ferrocyanide come down. The solution, after precipitation is complete, is still slightly acid. The *o*-compound is filtered off, washed with a little water, and a very little dilute hydrochloric acid. It is dried, and the base obtained from it by decomposing with caustic soda and extraction with ether. After drying the ethereal solution with potassium carbonate, and removing the ether, the base distils at 198°.




*Yield.*—90—95% theoretical (total *o* and *p*). *o*, B.P. 198°; D. 1·003; *p*, M.P. 45°; B.P. 200°; D. 1·046. (J. C. S., 121, 1294.) For preparation of *m*-toluidine, see J. S. C. I., 51, 283.

PREPARATION 361.—**α-Naphthylamine.**



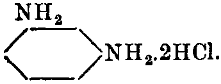

$C_{10}H_9N$. 143.

The reduction is similar to that of nitrobenzene (Preparation 359), but no condenser need be used in this case. 120 gms. iron powder and 60 c.cs. water are placed in the reduction pot, and the temperature raised to 95°. 10 c.cs. of conc. hydrochloric acid are then poured in and 100 gms. α-nitronaphthalene added gradually. The reduction is continued until a sample is completely soluble in hydrochloric acid.

*Separation.*—The steam distillation is carried out as in Preparation 359, using in this case superheated steam. A convenient apparatus for producing superheated steam is shown in Fig. 15. The naphthylamine is then filtered off and crystallised from benzene or toluene.

*Yield.*—80—85% theoretical (65—70 gms.). M.P. 51°; B.P. 300°; D. 1·23. A small percentage of β-naphthylamine is formed in the reduction. (J. pr., 27, 140; A., 92, 401; 275, 217.)

PREPARATION 362.—***m*-Phenylenediamine Hydrochloride.**




$C_6H_{10}N_2Cl_2$. 181.

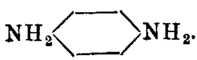
This process is carried out in the usual reduction pot with reflux attached (see Fig. 37).

150 c.cs. water are placed in the reduction pot and heated up to 95°, and 100 gms. *m*-dinitrobenzene (M.P. 91°) are then added. 10 c.cs. of conc. hydrochloric acid and about 120 gms. of fine iron powder are added gradually, care being taken that the contents do not froth over. This process is carried on until the solution loses its yellow colour, as may be shown by spotting on filter paper. A solution of sodium carbonate is then added until an alkaline reaction is obtained. It is boiled and filtered from the iron residue. The iron residue is again boiled with water and filtered. The combined filtrates are evaporated to a convenient bulk and conc. hydrochloric acid added to precipitate the hydrochloride. This is allowed to cool, and is filtered and dried.

The crude base obtained on evaporation of the above filtrate is too soluble to be crystallised from water, and is usually purified by vacuum distillation.

*Yield.*—90% theoretical (77 gms.). M.P. 61°; B.P. 283°. Very soluble in water. (J., 1861, 512; 1863, 422; Z. Ch., 1865, 51.)

PREPARATION 363.—***p*-Phenylenediamine.**



$C_6H_8N_2$. **108.**

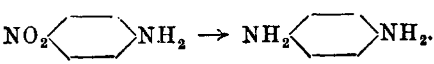
The process is similar to that used for making the *meta*-compound. In this case, however, *p*-nitroaniline is added to the mixture of iron powder, water, and acid. The following quantities are used :—

100 gms. iron powder; 5 c.cs. conc. hydrochloric acid; 100 c.cs. water.

These are heated to 95° and 100 gms. *p*-nitroaniline gradually added. Cooling may have to be applied to regulate the action.

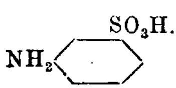
The reduction is continued as in Preparation 362 until the liquid loses its yellow colour.

Sodium carbonate is added, as before, until alkaline. After the iron residue is filtered off the filtrate is concentrated until the base crystallises.



*Yield.*—80% theoretical (60 gms.). M.P. 147°; B.P. 267°. (J., 1863, 422; B., 7, 871; 28, 250.)

PREPARATION 364.—**Metanilic Acid** (*Aniline*-m-*sulphonic acid*).

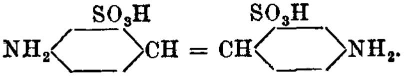


$C_6H_7O_3NS$. **173.**

123 gms. nitrobenzene are sulphonated (p. 314) and the sulphonation mixture reduced, using iron powder, as in H-acid (p. 315). After the reduction mixture is neutralised, the filtrate is concentrated to about 600 c.cs. Hydrochloric acid is added until an acid reaction to Congo is obtained. The metanilic acid then crystallises out. The separation may be assisted by adding common salt.

*Yield.*—80% theoretical. Crystallises with $\frac{1}{2}H_2O$ of crystallisation; intermediate for dyestuffs. (Z. a., 9, 686.)

PREPARATION 365.—**4 : 4′-Diaminostilbine-2 : 2′-disulphonic Acid.**



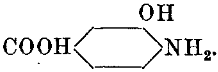
$C_{14}H_{14}O_6N_2S_2$. 370.

The sodium salt of the dinitro acid from Preparation 288 is dissolved in 300 c.cs. hot water, and hydrochloric acid is added to neutralise any free sodium carbonate. The solution is run on to 200 gms. of iron turnings, which have been previously etched by standing in 20 c.cs. of 40% acetic acid. The reduction proceeds in the normal way.

The solution is made strongly acid to Congo red with hydrochloric acid, and the diaminostilbinedisulphonic acid separates as yellow crystals. After 10 hours it is filtered off and washed.

*Yield.*—About 40% (calculated on *p*-nitrotoluene). Important intermediate for dyestuffs. (B., 30, 3100.)

PREPARATION 366.—**4-Amino-3-hydroxybenzoic Acid.**

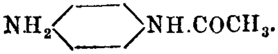


$C_7H_7O_3N$. 153.

10 gms. 4-nitro-3-hydroxy benzoic acid (see p. 269) and 200 c.cs. conc. hydrochloric acid are heated on a water bath, and 30 gms. of tin slowly added. After the reaction is complete the double tin salt separates out, and is filtered. The precipitate is dissolved in 200 c.cs. of warm water and hydrogen sulphide passed until all the tin is separated. The filtrate from the tin is concentrated until crystals of the hydrochloride begin to separate. When cold, the hydrochloride is filtered, dissolved in a little water, and the free base precipitated by the addition of a conc. solution of sodium acetate. It is filtered, washed with water, and recrystallised from hot water or dilute alcohol.

*Yield.*—60% theoretical (5 gms.). M.P. 115°—116°. (J. C. S., 119, 1429.)

PREPARATION 367.—***p*-Aminoacetanilide.**

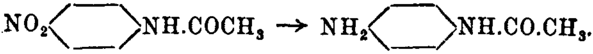


$C_8H_{10}ON_2$. 150.

93 gms. of aniline are converted into acetanilide, and then to nitroacetanilide, as shown in the preparation of *p*-nitroaniline (p. 275). The moist nitro compound is then added in small portions to a vessel fitted with good agitation (see Fig. 37), and containing 125 gms. iron filings, 8 c.cs. 40% acetic acid and 500 c.cs. water heated to boiling. Boiling is continued for 10 minutes after the last addition, when the solution "spotted" on filter paper should be colourless. The liquid is then cooled to 70°, and sodium carbonate is added until the reaction is alkaline.* The precipitation of the iron is completed by adding the minimum quantity of ammonium sulphide until a drop on filter paper gives no

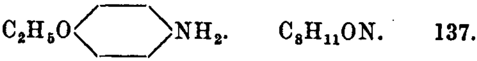
* If the sodium carbonate is added at 100° or in excess, hydrolysis of the aminoacetanilide takes place.

coloration with sodium sulphide. The whole is then filtered, and the filtrate evaporated to 400 c.cs., when, on cooling, the aminoacetanilide crystallises in long needles. A further crop of crystals may be obtained by evaporating the mother liquor.



*Yield.*—55% theoretical (80—90 gms.). M.P. 162·5°; on hydrolysis gives *p*-phenylenediamine. (B., 17, 343; A., 293, 373.)

PREPARATION 368.—**p-Phenetidine** (1-*Ethoxy*-4-*aminobenzene*).



1. p-*Nitrophenetole.*—140 gms. *p*-nitrophenol are dissolved in 400 gms. of 10% caustic soda solution, and the solution is placed in an enamel-lined autoclave fitted with a stirrer. 70 gms. ethyl chloride are introduced, and the mixture heated for 7—8 hours at 90°—100°. After cooling, the *p*-nitrophenetole is filtered off and washed with dilute caustic soda to remove unchanged nitrophenol, and then with water.

2. p-*Phenetidine.*—100 gms. *p*-nitrophenetole, 200 c.c. water and 10 c.c. conc. hydrochloric acid are placed in a flask or a sulphonating pot fitted with a good mechanical agitator (see Fig. 37). The temperature is raised to 60°, and iron filings (100 gms.) are gradually introduced over 3—4 hours. When all the iron has been added the temperature is raised to 90°, where it is maintained until the reduction is complete. The supernatant aqueous liquor is poured or siphoned off, and the sludge is steam distilled with superheated steam at 160°—180°, when the *p*-phenetidine passes over, and is separated from the aqueous distillate by extraction with ether, and purified by distillation.

Liquid; B.P. 244°. (Am. Soc., 1, 272; B., 22, 1782; U.S.P., 1890430.)

**Reaction CLXX. Action of Metals on Nitro Compounds in Alkaline Media.**—The metal usually employed is zinc, although iron powder can be used in some cases. The reaction is usually carried out in presence of caustic soda.

$$Zn + 2NaOH \rightarrow Zn(ONa)_2 + H_2,$$

and the reaction takes place in several stages.

$$\begin{array}{l} RNO_2 \\ RNO_2 \end{array} + 6H \rightarrow \begin{array}{l} R{-}N \\ R{-}N \end{array}\!\!>\!O \quad \text{or} \quad \begin{array}{c} R.N = N.R \\ \downarrow \\ O \end{array} \quad \text{azoxy—}$$

$$\begin{array}{l} R{-}N \\ R{-}N \end{array}\!\!>\!O + 2H \rightarrow \begin{array}{c} R{-}N \\ \| \\ R{-}N \end{array} \quad \text{azo—}$$

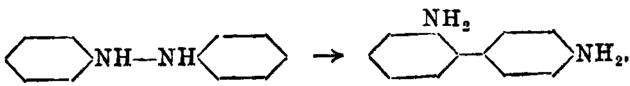
$$\begin{array}{c} R{-}N \\ \| \\ R{-}N \end{array} + 2H \rightarrow \begin{array}{c} R.NH \\ | \\ R.NH \end{array} \quad \text{hydrazo—}$$

A slight excess of metal is required, and each stage can be isolated by using the required amount of metal, *e.g.*, 3 atoms, for the azoxy-, 4 for the azo-, and 5 for the hydrazo-stage. A certain amount of primary amine is also formed.

Good agitation is essential, and a solvent may be used in some cases. This, however, is not always necessary if the agitation is efficient. The compounds are isolated by dissolving out the zinc with *ice-cold* hydrochloric acid. The hydrazo compounds, when heated with mineral acids, undergo a rearrangement (benzidine conversion).

$$C_6H_5.NH—NH.C_6H_5 \rightarrow NH_2C_6H_4—C_6H_4NH_2.$$

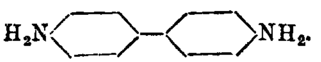
the $NH_2$ groups taking the *p*-position, although a certain amount of *o-p*-compound is formed,




as well as *o*- and *p*-semidines (see p. 160).

The sulphates of these last compounds are soluble in water, and they can, therefore, be separated from the *p-p'*-compounds by means of sodium sulphate or sulphuric acid.

PREPARATION 369.—**Benzidine** (4 : 4'-*Diamino-diphenyl*).




$C_{12}H_{12}N_2$. 184.

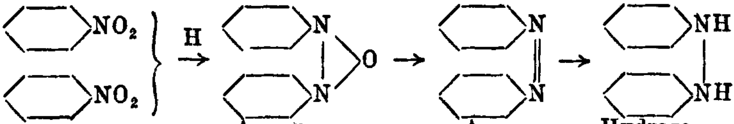
1. *Hydrazobenzene.*—100 gms. nitrobenzene, 100 gms. of conc. caustic soda (30% solution) and 100 gms. water are placed in the reduction pan (see Fig. 37) and heated to 95°, and all external heat cut off. Zinc dust of good quality (over 85% metallic zinc) is then added, a few gms. at a time. The heat of reaction will raise the temperature to 100°, and when it cools to 98° a few more gms. of zinc dust are added, the temperature being allowed to drop to 98° before any further addition of zinc is made.

During the course of the reduction small samples are abstracted by means of a rod. It will be noticed that at first a yellowish-red crystalline solid is formed on the rod, then a red crystalline solid, and ultimately all trace of red disappears and a lemon-yellow crystalline solid is formed. When this stage is reached further addition of zinc is stopped, and the whole is allowed to run for ½ hour, external heat being applied. In all about 160 gms. of zinc dust will be necessary, the amount, of course, depending on the metallic content of the dust.

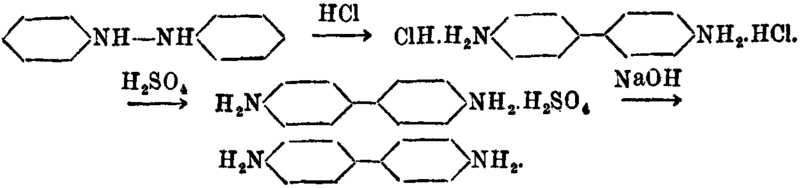
The whole is quickly cooled by adding a large bulk of cold water to the reduction pot, agitation being maintained.

When cooled to 30°, the contents of the pot are poured into a large enamelled bucket. A large quantity of ice is added, and conc. hydrochloric acid is poured in, with stirring. The temperature should not rise above 5°. Acid is added until the liquid in the bucket gives an acid reaction to Congo paper. The hydrazobenzene is then filtered off and washed with cold water.

2. *Benzidine.*—It is then removed to a basin where it is boiled up slowly with 500 c.cs. water and 120 c.cs. conc. hydrochloric acid and filtered from zinc residue. A saturated solution of sodium sulphate is then added until the benzidine sulphate is completely precipitated (test). This is filtered off and is well washed with warm water until free of acid. The moist benzidine sulphate is removed, heated to 50° with a little water, and caustic soda solution (30%) added with stirring until the liquid is just alkaline (test with phenolphthalein). When cold, the free base is filtered off and dried at 50°. It may be crystallised from benzene, alcohol or from hot water (see p. 498).

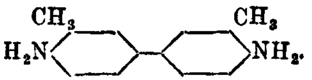


Azoxy (yellow-red) M.P. 36°. | Azo (red) M.P. 68° | Hydrazo (white) M.P. 131°



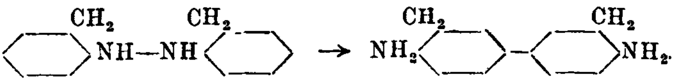
*Yield.*—75—80% theoretical (55—60 gms.). Lustrous plates; M.P. 128°; monohydrate M.P. 105°; B.P. over 400°, with decomposition; slightly soluble in hot water; soluble in alcohol and in benzene. Important intermediate for dyestuffs. (Z. a., 6, 67.)

PREPARATION 370.—***o*-Tolidine** (*4 : 4′-Diamino-3 : 3′-dimethyldiphenyl*).



$C_{14}H_{16}N_2$. 212.

The process is exactly the same as for benzidine, except that 100 gms. of distilled *o*-nitrotoluene (containing not more than 4% *p*-nitrotoluene) are used.



*Yield.*—65% theoretical (48 gms.). Plates; M.P. 128°; slightly soluble in water; soluble in alcohol and in benzene; salts about 5 times more soluble than those of benzidine; intermediate for dyestuffs. (B., 17, 467; 20, 2017.)

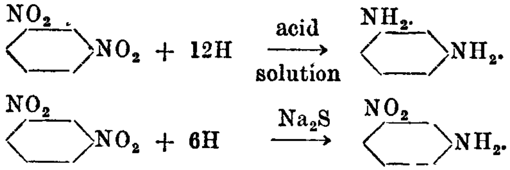
**Reaction CLXXI. Action of Alkali Sulphides and Hydrosulphides on Nitro Compounds.**

$$R.NO_2 \rightarrow R.NH_2.$$

The hydrogen is generated in the solution of alkali sulphide.

$$Na_2S + 3H_2O \rightarrow Na_2SO_2 + 3H_2.$$

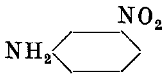
Excess of $Na_2S$ is used, which dissolves the sulphur always formed in the reaction, due to oxidation. The reaction is specially useful in cases of nitro compounds containing more than one nitro group, and conditions can be chosen such that only one nitro group is reduced, *e.g.*,



The reaction is really an extension of that on alkaline reduction, since the solution of sodium sulphide in water is alkaline. The complete equations are :

$$R.NO_2 + Na_2S + H_2O \rightarrow R.NH_2 + Na_2SO_3$$
$$4R.NO_2 + 6NaSH + H_2O \rightarrow 4R.NH_2 + 3Na_2S_2O_3.$$

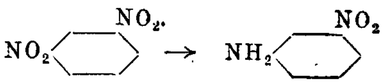
PREPARATION 371.—*m*-**Nitroaniline.**



$C_6H_6O_2N_2$. 138.

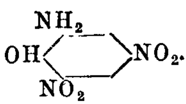
This experiment should be performed in a fume cupboard.

100 gms. *m*-dinitrobenzene are placed in a beaker with 500 c.cs. water and heated to 85°. The stirring should be very brisk. 245 gms. sodium sulphide ($Na_2S.9H_2O$) dissolved in 200 c.cs. water are then allowed to drop in from a funnel during 10 minutes. The dinitrobenzene is reduced to *m*-nitroaniline. The end of the reaction may be recognised by "spotting" the solution on filter paper, and touching with iron or copper sulphate solution. When the black stain remains for 20 seconds, the reduction is finished and the mixture is cooled down to 20° by adding ice. After standing for several hours the *m*-nitroaniline is filtered off, and may be recrystallised from boiling water.



*Yield.*—70% theoretical (58 gms.). M.P. 112·4° ; B.P. 285° ; intermediate for azo dyestuffs. (C. Z., 37, 299.)

PREPARATION 372.—**Picramic Acid** (2-*Amino*-4 : 6-*dinitrophenol*).



$C_6H_5O_5N_3$. 199.

10 gms. picric acid and 3·5 gms. of caustic soda are dissolved in 600 c.cs. water in a large flask and heated up to 55° with vigorous stirring, when a solution of 40 gms. crystalline sodium sulphide ($Na_2S.9H_2O$) in 100 c.cs. water is gradually added.

127·5 gms. of powdered picric acid are then gradually added concurrently with 220 gms. sodium sulphide in 400 c.cs. of water. The addition

of the picric acid should end at the same time as the sulphide solution. The temperature should not rise above 65°, ice being added, if necessary. Stirring is continued for about 10 minutes after this addition, and then 400 gms. ice are introduced. The sodium salt of picramic acid is immediately precipitated. After standing for 10 hours it is filtered off and washed with brine.

The free acid is obtained by stirring up the sodium salt with 500 c.cs. water, heating to 80°, and acidifying with dilute sulphuric acid until just acid to Congo red.

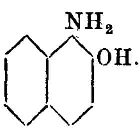
*Yield.*—90% theoretical (100 gms.). Red needles, soluble in water; M.P. 168°—169°. (See also A., 88, 281; 96, 83; J. Soc. Dyers., 46, 365.)

**Reaction CLXXII. Action of Reducing Agents on Azo Compounds.**—

$$X{-}N = N{-}Y \xrightarrow{H_2} X.NH_2 + H_2N.Y.$$

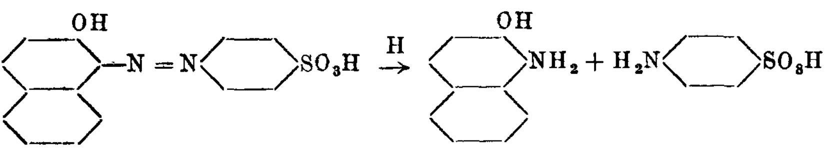
This reaction is useful for determining the composition and constitution of azo dyes. The reducing agents employed are usually metal and acid, zinc dust and water or ammonia, stannous chloride, or sodium hydrosulphide in alkaline solution. The reaction is carried out with or without heat, until the suspended or dissolved colour gives place to a colourless product containing one or two primary amines.

PREPARATION 373.—**α-Amino-β-Naphthol.**



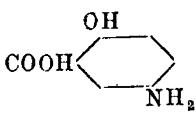
$C_{10}H_9ON$. 159.

50 gms. Orange II. (see Preparation 386) are dissolved in 500 c.cs. boiling water, and to this are added 65 gms. tin dissolved in 375 c.cs. conc. hydrochloric acid. When decolorisation is complete the solution is filtered quickly and on cooling the hydrochloride of amino-naphthol separates out as colourless crystals.



Fine needles, slightly soluble in dilute hydrochloric acid and in alcohol. (B., 25, 980.) See also O. S., XI., 8.

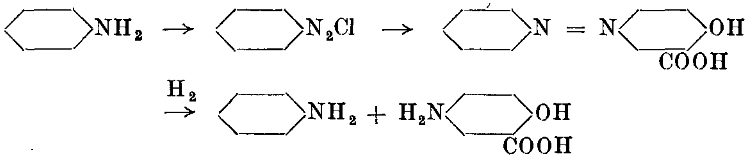
PREPARATION 374.—**Aminosalicylic Acid** (2-*Hydroxy*-5-*aminobenzoic Acid*).



$C_7H_7O_3N$. 153.

A mixture of 50 gms. of aniline hydrochloride, 60 gms. of conc. hydrochloric acid, and 300 gms. of ice is diazotised by adding a solution of 29 ms. of sodium nitrite in 100 c.cs. of water to the mixture. After

15 minutes the diazonium salt is run into a solution of 53·3 gms. of salicylic acid in 220 gms. of crystallised sodium carbonate and a litre of water. The sodium salt separates, is filtered and washed with a little water. The azo compound is next boiled with about a litre of water, sodium hydroxide solution added until alkaline and dry sodium hyposulphite (about 135 gms.) added until the reduction is complete. After the aniline is removed by steam distillation, acid is added, and the free amino-salicylic acid separates.



Decomposes at 280°. (B., 32, 81.) See also Abs. B., 1936, 440.

**Reaction CLXXIII. Action of Reducing Agents on Nitroso Compounds.**

$$R.NO \longrightarrow R.NH_2.$$

The reduction to a primary amine is usually carried out in acid solution, or with bisulphite. For example, see Preparation 393.

**Reaction CLXXIV. Reduction of Oximes to Amines with Metallic Sodium or Sodium Amalgam.**

$$>C:NOH \xrightarrow{4H} >CH.NH_2 + H_2O.$$

The reaction serves for the production of amines from aldehydes or ketones through the oximes of these bodies.

Reduction with metallic sodium is usually carried out in absolute alcoholic or moist ethereal solution. Methyl, ethyl or amyl alcohol may be used, but for various reasons absolute ethyl alcohol is the most frequently employed, the reaction being conducted at or near the boiling point of the alcohol. When ordinary alcohol (about 90%) is used, the sodium spurts about on the surface of the liquid, and most of the hydrogen escapes as gas. With the absolute alcohol, the sodium—with the exception of the first portions added—melts to a ball which remains largely, and at times completely, immersed in the liquid, and hence the hydrogen generated is more liable to react. In some cases the sodium alcoholate formed also acts as a reducing agent, and is thereby converted into the sodium salt of the corresponding acid.

When the reduction is carried out with sodium amalgam the oxime is dissolved in aqueous alcohol, and acetic acid and amalgam added at intervals so that the solution is slightly acid throughout the reduction.

PREPARATION 375.—**α-Phenylethylamine** [1-*Phenyl*-1-*amino-ethan*].

$$C_6H_5CH(NH_2)CH_2. \qquad C_8H_{11}N. \qquad 121.$$

50 gms. acetophenone oxime dissolved in 100 c.cs. absolute ethyl alcohol are placed in a litre round-bottomed flask having a long neck. The flask is fitted with a cork carrying an addition tube (p. 50), and the

sloping limb of the latter is attached to a reflux water condenser, while the vertical limb is closed with a cork. A bottle containing benzene and pieces of bright sodium (about 50 gms.) of such a size that they slip easily down the addition tube is prepared. The flask is heated on a water bath until the alcohol boils. Pieces of sodium (one at a time) are introduced through the vertical limb of the addition tube, a piece of drawn-out glass rod being used to remove the sodium from the bottle, and the benzene adhering need not be removed with filter paper. The first pieces of sodium cause vigorous reaction, but the reaction soon becomes moderate. The alcohol is kept actively boiling all the time. When the reaction becomes sluggish a further 100 c.cs. absolute alcohol are added, and addition of sodium to the boiling solution is continued, as before. Altogether about 500 c.cs. absolute alcohol and 40 gms. sodium are required. The addition of sodium is continued until a test, carried out in the following way, shows that reduction is complete :—

A sample (about 2 c.cs.) is withdrawn, diluted with an equal volume of water, and about 2 c.cs. conc. hydrochloric acid added. The mixture is boiled for a minute with Fehling's solution (1) prior to the addition of an excess of Fehling's solution (2) (see p. 499). If no reduction of the Fehling's solution takes place the reduction of the oxime is complete.

When reduction is complete and all the sodium dissolved, the flask is cooled, and 200 c.c. water added to decompose the ethoxide. A sloping condenser is then attached and heating continued on a water bath until distillation slackens. A further 200 c.c. water are then added and heating continued on a sand bath until all the alcohol has passed over and a thermometer inserted in the neck of the flask registers 96°. The contents of the flask, consisting of a layer of amine and a layer of caustic soda, are cooled and poured into a separating funnel. A little ether is used to complete the transference of the amine. The total distillate, containing alcohol, water, and α-phenylethylamine, is made strongly acid with hydrochloric acid and evaporated to small bulk, after which the residual aqueous solution of amine hydrochloride is added to the contents of the separating funnel, where the excess of caustic soda liberates the base. After some time the lower layer of caustic soda is run off, the upper layer of amine is agitated with 20 c.c. 0·720 ether, and the final traces of caustic soda separated. The products from the reduction of a number of 50 gms. instalments of acetophenoneoxime may with advantage be united at this stage. The ethereal solution along with ethereal washings is dried over anhydrous sodium sulphate and distilled. At first ether containing some amine passes over—this portion of distillate which is alkaline to litmus is kept separate for recovery as carbamate. The temperature then rises rapidly to 186°—187°, at which the amine distils; the condenser, which should be long, is only half-filled with water at this stage. Owing to the avidity of the amine for carbon dioxide it should be collected in a flask having a soda-lime side tube.

$$C_6H_5C(NOH).CH_3 \longrightarrow C_6H_5.CH(NH_2).CH_3.$$

$$2C_6H_5CH(NH_2)CH_3 + CO_2 \longrightarrow C_6H_5CH(CH_3)NHCOONH_3CH(CH_3).C_6H_5.$$

*Yield.*—90% theoretical (40 gms.). Dry carbon dioxide passed into the dry ethereal distillate causes precipitation of a quantity of carbamate, which increases the yield to 95%.

*α-Phenylethylamine.*—B.P. 186°; easily soluble in organic solvents; moderately soluble in water; strong base; absorbs carbon dioxide when exposed to air. (For resolution see p. 408.)

*α-Phenylethylamine Carbamate.*—M.P. 101°—102°; easily soluble in water or in alcohol; on heating, dissociates into amine and carbon dioxide. (J. C. S., 83, 1147; 1928, 2483; J. R. T. C., 1926, 59.)

*Catalytic Reduction of Oximes.*—Oximes may be reduced to primary amines in good yield by hydrogen in presence of nickel-kielselgühr (p. 172). (Am. Soc., 55, 1669).

# CHAPTER XXIV

## HYDROGEN TO NITROGEN

### Hydroxylamines and Hydrazines

**Reaction CLXXV. Action of Metallic Zinc on Nitro Compounds in Neutral Media.**

$$R.NO_2 + 4H \rightarrow R.NHOH,$$

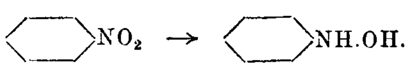
*e.g.*, nitrobenzene gives phenylhydroxylamine. Although the reaction may be carried out by generating the hydrogen by the interaction of zinc and water, better yields are obtained by adding a neutral salt, such as ammonium chloride. In order to prevent the reduction going beyond this stage it is necessary to keep down the temperature. (B., 27, 1432, 1548 ; D. R. P., 84, 138.)

If the reduction is carried out in presence of alcohol at 70°—75°, azoxy-, azo-, and, in some cases, hydrazo-compounds can be obtained. These reductions take place *viâ* intermediate organo-zinc salts which decompose yielding the azoxy-compound, etc., and a double basic zinc salt of the formula, $2NH_4Cl, 5Zn(OH)_2$. (J. C. S., 123, 2466 ; 125, 1108 ; J. R. T. C., 1929, 43 ; 1930, 191.)

Preparation 376.—**Phenylhydroxylamine** ((*Hydroxy-amino*)-*benzene*).

$$C_6H_5NHOH. \qquad C_6H_7ON. \qquad 109.$$

12 gms. of nitrobenzene are mixed in a beaker with 250 c.cs. of water containing 6 gms. of ammonium chloride and well stirred, the temperature being kept at 10°—15°. 18 gms. of good zinc dust are added in four equal parts after intervals of $\frac{1}{4}$ hour. When the smell of nitrobenzene has disappeared the stirring is stopped. The mixture is filtered at the pump, the filtrate being put on one side, and the precipitate washed, by adding 200 c.cs. of water at 45° while the pump is not working, and then the water gradually sucked through by means of the pump. The filtrate and the washings are separately saturated with sodium chloride, and cooled to 0°. After a short time the phenylhydroxylamine separates out ; it is filtered and dried without washing.



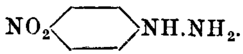

*Yield*.—65% theoretical (7 gms.). Colourless crystals ; M.P. 81°. (D. R. P., 89978 ; J. C. S., 123, 2464 ; Am. Soc., 45, 1784 ; O. S., IV., 56.)

**Reaction CLXXVI. Action of Reducing Agents on Diazonium Compounds.**

$$RN = NCl + 4H \rightarrow R.NH.NH_2.$$

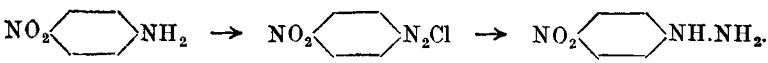
The reaction is somewhat similar to that (CLXXII.) of reducing agents on azo-compounds. The hydrazines are universally obtained by this reaction, the same reducing agents being used as in the case of azo-compounds.

PREPARATION 377.—***p*-Nitrophenylhydrazine.**




$C_6H_7O_2N_3$. **153.**

10 gms. *p*-nitroaniline are diazotised (p. 372). The filtered diazonium solution is slowly added, with stirring, to 40 c.cs. of a cold saturated solution of ammonium sulphite (see p. 512) containing 8 c.cs. of conc. ammonia solution. Ammonium nitrophenylhydrazine disulphonate soon separates, and after standing for about an hour in a freezing mixture is filtered, and the precipitate heated on the water bath with 20 c.cs. conc. hydrochloric acid for a few minutes at 70°—80°. The solution obtained is cooled in ice, and the precipitate which separates is dissolved in a small quantity of water. To this solution a cold concentrated solution of sodium acetate is added; the nitrophenylhydrazine separates and is recrystallised from alcohol.




*Yield.*—15—20% theoretical (2 gms.). Orange-red needles; M.P. 157°, with decomposition; soluble in alcohol and in ligroin. (J. C. S., 121, 719.)

PREPARATION 378.—**Phenylhydrazine.**

$C_6H_5NH.NH_2$. $C_6H_8N_2$. 108.

*Method I.*—10 gms. freshly distilled aniline are added to a solution of 30 gms. conc. hydrochloric acid in 75 c.cs. water and diazotised with 8 gms. sodium nitrite in 30 c.cs. water, the temperature being kept about 0°. 30 gms. common salt are added with shaking, and the solution cooled in a freezing mixture. 60 gms. stannous chloride in 25 gms. conc. hydrochloric acid are then added, and after standing for some hours the hydrochloride of phenylhydrazine separates, is filtered off and washed with a little saturated salt solution. It is transferred to a flask and treated with excess of caustic soda solution, when the free base is extracted with ether. The ethereal solution is dried with caustic potash, and the ether removed by evaporation. The phenylhydrazine may be purified, if desired, by freezing or by distilling *in vacuo*.

$$C_6H_5NH_2 \longrightarrow C_6H_5N_2Cl \xrightarrow{H_2} C_6H_5NH.NH_2.HCl.$$

*Yield.*—90% theoretical (10 gms.).

*Method II.*—10 gms. aniline are dissolved in acid and water and diazotised as before. The diazonium solution is poured into a saturated solution of sodium sulphite containing 34 gms. $Na_2SO_3$. The liquid is now heated with zinc dust and a little acetic acid till it becomes colourless,

when it is filtered hot. Sodium phenylhydrazine sulphonate passes into the filtrate, and is immediately mixed with one-third of its volume of fuming hydrochloric acid (*caution !*) which converts it into phenylhydrazine hydrochloride, which is thrown out of solution, filtered, and well pressed. The free base is liberated as before.

*Yield.*—75% theoretical (8 gms.). Colourless crystals; M.P. 23°; B.P.$^{760}$ 243·5° (decomposition); B.P.$^{12}$ 120°; soluble in alcohol, ether, benzene. (B., 16, 2976; 26, 19; 31, 346; O. S., II., 71.)

# CHAPTER XXV

## THE LINKING OF NITROGEN TO NITROGEN

### Diazonium Compounds

**Reaction CLXXVII. Action of Nitrous Acid on Primary Aromatic Amines.**

Diazonium compounds are formed in this way.

$$C_6H_5NH_2 + HNO_2 + HCl \longrightarrow \underset{\overset{|||}{N}}{C_6H_5NCl} + 2H_2O.$$

$$C_6H_5NH_2 + NaNO_2 + 2HCl \longrightarrow \underset{\overset{|||}{N}}{C_6H_5NCl} + NaCl + 2H_2O.$$

Diazonium compounds are usually prepared in mineral acid solution, and the nitrous acid generated from sodium nitrite. Sufficient acid must be used to generate nitrous acid and to form the salt of the base, and still leave the solution acid. In practice $2\frac{1}{4}$—$2\frac{1}{2}$ mols. of hydrochloric acid are generally employed. In most cases it is essential that the reaction be carried out at about 0°, as many diazonium solutions decompose above this temperature. The reaction goes very readily in some cases ; but in others, and especially where an acid group is present, *e.g.*, naphthylamine sulphonic acids, the reaction is only carried out with difficulty. It is possible to diazotise a solid in suspension, but the reaction is usually very slow. If the solid is dissolved and reprecipitated in a fine state of division the action goes much more quickly.

In the case of acidic substances, the compound is dissolved in sodium carbonate or caustic soda solution, and reprecipitated with the requisite amount of acid and then diazotised.

Commercial sodium nitrite contains 1—3% sodium nitrate, the harmful effect of which on diazonium compounds may be obviated by adding to the amine solution or the nitrite solution an amount (1·5—4·5% of the weight of nitrite used) of sodium metabisulphite slightly in excess of that necessary to reduce the nitrate. Diazonium compounds prepared in this way or with pure sodium nitrite are much more stable (J. Soc. Dyers, 41, 275.)

**Diazotisation.**—In the ordinary process of diazotisation the base is dissolved in the requisite quantity of acid, with heating if necessary, and excess of ice is added to bring the temperature down to 0°—5°. Sodium nitrite in the form of a 10% solution is then run in until the end point is reached.

*The End Point.*—The reaction is complete when on stirring after each addition, and testing with starch-iodide solution or paper, a distinct blue colour is obtained at once. A drop of the solution is removed on a glass rod at intervals and placed on the starch-iodide paper, or on a piece of dry filter paper near a drop of starch-iodide solution (see p. 504). Whenever the blue colour is obtained, and this colour persists when another test is made after 3 minutes, the reaction is complete. A blue colour developed on the paper after a time is disregarded. The nitrite should be added at such a rate that no free nitrous acid is evolved. It is essential that the starch-iodide solution or paper should be tested with a very dilute acidified solution of sodium nitrite before use.

It is not usually necessary to isolate the diazonium salt from solution, although in some cases this separates out as the reaction proceeds. If sufficient acid is not present, an aminoazo compound may be precipitated, due to the "coupling" (see p. 282) of the diazonium compound with the excess of base. In fact, this is one method of forming aminoazo compounds—by diazotising in presence of about half the quantity of acid necessary for the complete diazotisation.

In certain instances when negative substituents are present it is necessary to use other acids in place of hydrochloric to bring about diazotisation, *e.g.*, nitrosylsulphuric acid, in presence of conc. sulphuric (J. pr., 56, 48), in glacial acetic (J. C. S., 1933, 1620), in phosphoric acid (Am. Soc., 1933, 4531).

*Stabilised diazo compounds* can be prepared (*a*) as diazonium sulphates or chlorides, *e.g.*, tetrazotised *o*-dianisidine, (*b*) as complex salts with metallic halides, *e.g.*, $RN_2Cl, ZnCl_2$; (*c*) as diazoaryl sulphonates,

$$RN_2X + R_1SO_3H \rightleftharpoons RN_2OSO_2R_1,$$

(*d*) as mixtures of dry components, *e.g.*, amine salt, acid salt and sodium nitrite.

For further information see "Aromatic Diazo Compounds" by Saunders, Chap. 2.

PREPARATION 379.—**Diazonium Compounds (in Solution).**

1. *Aniline* $C_6H_5N_2Cl$.

9·3 gms. aniline are run into 100 gms. of water and 45 gms. conc. hydrochloric acid. 100 gms. ice are added, and the whole is stirred till temperature reaches 0°. 7 gms. sodium nitrite (as a 10% solution) are then gradually added, preferably by a tube leading under the surface of the solution.

The temperature should not rise above 7°—8°. Slow stirring is continued all the time, except when tests are being made. When a distinct blue colour is obtained on starch-iodide paper at once, which persists after another test in 3 minutes, the diazotisation is complete.

2. *Benzidine* $ClN_2C_6H_4—C_6H_4N_2Cl$. *or Tolidine*

The process is similar to above, 18·4 gms. benzidine or 21·2 gms. tolidine being dissolved by heating in 300 gms. water and 90 gms. conc. hydro-

chloric acid. After cooling to 0°, the diazotisation is carried out as before. In these cases tetrazonium compounds are formed.

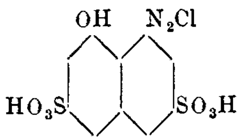
3. *p-Nitroaniline.*

$$NO_2C_6H_4N_2Cl.$$

(*a*) 13·8 gms. *p*-nitroaniline are powdered and added to a mixture of 150 gms. water, 45 gms. conc. hydrochloric acid, and 150 gms. ice, and stirred for 15 minutes, the temperature being under 5°. 7 gms. sodium nitrite (10% solution) are introduced *quickly*, the usual test with starch iodide being applied after all of the nitrite solution has been added.

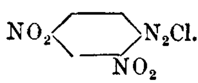
(*b*) 13·8 gms. *p*-nitroaniline are added to 70 gms. water and 45 gms. conc. hydrochloric acid, and heated to dissolve. The solution is then cooled and diazotised, as before.

4. *H Acid.*




34·1 gms. H-Acid are introduced into 400 gms. water and 6 gms. sodium carbonate at a temperature of 40°—50°. The solution should be alkaline. This is run into a mixture of 55 gms. hydrochloric acid and 500 gms. water. The mixture is cooled to 5°, and 7 gms. sodium nitrite (10% solution) are then added—as before—slowly towards the end.

5. *Dinitroaniline.*




8 gms. sodium nitrite are dissolved in conc. sulphuric acid by heating to about 50°. The solution is cooled to 20°, and 18·3 gms. finely powdered dinitroaniline are gradually added. When all has been added, stirring is continued for 2 hours at 20°—30°. The solution is then poured on to ice and filtered. The diazonium compound is thus isolated as a paste.

PREPARATION 380.—**Diazoaminobenzene** (*Benzeneazoanilide*).

$$C_6H_5N = N.NH.C_6H_5. \qquad C_{12}H_{11}N_3. \qquad 197.$$

6 gms. of sulphuric acid and 600 c.cs. of water are placed in a litre beaker, and 20 gms. of aniline added. The solution is warmed to 30°, and a solution of 7·5 gms. of sodium nitrite dissolved in a little water added with constant stirring. The solution is maintained at 30° for 15 minutes, after which it is left to stand for 30 minutes at laboratory temperature. The diazoaminobenzene is then filtered off, washed with water, and dried on a porous plate. It may be recrystallised from warm petroleum, but the solution should not be boiled for any length of time as the compound is thereby decomposed.

$$C_6H_5N(\vdots N).HSO_4 + NH_2.C_6H_5 \rightarrow C_6H_5N : N.NHC_6H_5 + H_2SO_4.$$

*Yield.*—80% theoretical (17 gms.). Golden-yellow plates; M.P. 96°; explodes when heated slightly above its M.P.; O. S., XIV., 24.

PREPARATION 381.—**Diazobenzene Sulphate** (*Benzene Diazonium Sulphate*).

$$C_6H_5.N(\vdots N).SO_4H. \qquad C_6H_6O_4N_2S. \qquad 202.$$

15 gms. (1 mol.) of aniline and 140 gms. of *absolute* alcohol are mixed, and 30 gms. (2 mols.) of conc. sulphuric acid run in, slowly and with constant shaking. The precipitate of aniline sulphate, which first appears, redissolves. The mixture is kept at 30°—35° (thermometer in liquid), out of direct sunlight, while 20 gms. (1 mol.) of amyl nitrite are dropped in from a tap funnel. The whole is then left in ice-water for $\frac{1}{2}$ hour, and the crystals which have separated filtered off at the pump and washed with a little alcohol. As diazobenzene sulphate is explosive the precipitate must be kept moist. In that state it can be used for the various reactions described below.*

$$(C_6H_5NH_2)_2H_2SO_4 + 2C_5H_{11}ONO + H_2SO_4 = \\ 2C_6H_5N(\vdots N)SO_4H + 2C_5H_{11}OH + 2H_2O.$$

Colourless needles; soluble in water and methyl alcohol; slightly soluble in ethyl alcohol; on heating decomposes explosively at about 100°. (A., 137, 47; B., 28, 2049.)

PREPARATION 382.—**Diazobenzene Nitrate** (*Benzene Diazonium Nitrate*).

$$C_6H_5.N(\vdots N).NO_3. \qquad C_6H_5O_3N_3. \qquad 167.$$

Owing to the highly explosive nature of the diazobenzene nitrate, its preparation should never be undertaken except the compound is wanted for research or some special purpose. 20 gms. of aniline are placed in a beaker, well cooled, and "boiled-out" nitric acid, previously diluted with half its volume of water, carefully added till the mixture sets to a thick crystalline paste—aniline nitrate. The crystalline mass is filtered off at the pump, and washed with a little cold water. 5 gms. of the moist salt are finely powdered and placed in a small flask with enough water just to cover the substance. The flask is now well cooled in ice-water, and nitrous fumes (for preparation, see p. 513) are led in with frequent agitation until all the aniline nitrate has disappeared. At no time must the temperature of the flask rise above 10°. Should there not be sufficient water to keep all the diazobenzene nitrate formed in solution, its crystalline form will easily enable it to be distinguished from the aniline salt. When the reaction is finished the contents of the flask are poured into 3 times their volume of absolute alcohol, and ether is added to this mixture as long as crystals separate. If too much water has been added to the aniline nitrate from the beginning, a thick aqueous solution of diazobenzene nitrate separates out in place of the crystals. If this occurs, the ether-alcohol is decanted off, and the residue redissolved in absolute alcohol, and reprecipitated with ether. On no account must

* Any of the diazonium compound which remains over should be dissolved in water and poured away.

large quantities of the preparation be allowed to dry. If it has to be preserved it must be kept moist, or, better, in aqueous solution. The usual diazo reactions can be carried out with the latter.

$$C_6H_5.NH_2 + HNO_3 = C_6H_5NH_3.NO_3.$$
$$2C_6H_5.NH_3.NO_3 + NO + NO_2 = 2C_6H_5.N(\vdots N).NO_3 + 3H_2O.$$

Colourless needles; extremely explosive in the dry state; very soluble in water; insoluble in ether; on heating decomposes explosively. (A., 137, 41.)

**Reactions of Diazonium Compounds**

The following reactions are performed with about 1 gm. of moist diazobenzene sulphate. Some of the reactions are illustrated by preparations.

1. The substance is heated with a few c.cs. of ethyl alcohol, when vigorous effervescence takes place, and the liquid turns red. On adding water an oil consisting of benzene and a little phenetole separates on the surface.

$$C_6H_5.N_2.SO_4H + C_2H_5OH = C_6H_6 + N_2 + CH_3.CHO + H_2SO_4.$$
$$C_6H_5.N_2.SO_4H + C_2H_5OH = C_6H_5.O.C_2H_5 + N_2 + H_2SO_4.$$

2. A solution of about 1 gm. of the substance in a little water is cooled in ice, made alkaline with caustic soda, and treated with a cold, alkaline solution of stannous hydrate, made by treating about 4 gms. of stannous chloride in twice its weight of water, and adding 40% caustic soda solution until the precipitate redissolves. Effervescence occurs, nitrogen is liberated, and benzene separates on the surface of the liquid.

$$C_6H_5.N_2.ONa + Sn(ONa)_2 + H_2O = C_6H_6 + O : Sn(ONa)_2 + N_2 + NaOH.$$

3. An aqueous solution of the substance is gently warmed, when a vigorous evolution of nitrogen occurs, and a dark coloured oil, smelling strongly of phenol, separates. It can be extracted with ether and tested for phenol (see Preparation 352).

If a solution of diazobenzene nitrate be used, the liberated nitric acid acts on the phenol as it is formed, and nitrophenol is produced.

$$C_6H_5.N_2.SO_4H + H_2O = C_6H_5OH + H_2SO_4 + N_2.$$
$$C_6H_5.N_2.HNO_3 + H_2O = C_6H_5OH + HNO_3 + N_2.$$
$$C_6H_5OH + HNO_3 = C_6H_4(OH)(NO_2) + H_2O.$$

4. An aqueous solution of the substance is mixed with a solution of bromine in hydrobromic acid or potassium bromide, when a reddish-brown oil separates. This solidifies to a mass of leafy crystals, if the aqueous layer is poured off the oil, and the latter washed with a little ether. The crystals are diazobenzene perbromide.

$$C_6H_5.N_2.SO_4H + KBr + Br_2 = C_6H_5NBr.NBr_2 + KHSO_4.$$
$$C_6H_5.N_2.SO_4H + HBr + Br_2 = C_6H_5.NBr.NBr_2 + H_2SO_4.$$

If a sufficient quantity of the crystals has been prepared, it may be divided into two portions. One portion is covered with conc. ammonia. A violent reaction sets in, the crystals disappear, and a dark oil, possessing

a peculiar narcotic odour, is produced, consisting principally of benzene diazoimide.

$$C_6H_5NBrNBr_2 + NH_3 = C_6H_5N_3 + 3HBr.$$

The other portion of the perbromide is warmed with a little alcohol. Nitrogen and bromine are given off, and bromobenzene is formed.

$$C_6H_5.NBr.NBr_2 = C_6H_5Br + N_2 + Br_2.$$

5. Potassium iodide solution is added to an aqueous solution of the diazonium salt. Nitrogen is evolved, and a dark coloured oil, iodobenzene, separates.

$$C_6H_5.N_2.SO_4H + KI = C_6H_5I + N_2 + KHSO_4.$$

For large scale reaction see Preparation 338.

6. The solution of the diazonium salt is mixed with an aniline salt and excess of sodium acetate, or the solution is shaken up with a few drops of aniline. In either case a yellow crystalline precipitate of diazoaminobenzene is obtained.

$$C_6H_5.N_2.SO_4H + C_6H_5NH_2.HCl + CH_3COONa =$$
$$C_6H_5N : N.NHC_6H_5 + NaHSO_4 + CH_3COOH + HCl.$$
$$C_6H_5.N_2.SO_4H + C_6H_5NH_2 = C_6H_5N_2.NHC_6H_5 + H_2SO_4.$$

For large scale reaction see p. 374.

7. A solution of phenol in caustic soda is added drop by drop to an aqueous solution of the substance. An orange crystalline precipitate of sodium hydroxyazobenzene is formed. If $\beta$-naphthol be used in place of phenol a scarlet precipitate of sodium hydroxy-$\beta$-naphthaleneazobenzene is obtained.

$$C_6H_5.N_2.SO_4H + C_6H_5(ONa) = C_6H_5N : NC_6H_4(ONa) + Na_2SO_4 + 2H_2O.$$
$$C_6H_5.N_2SO_4H + C_{10}H_7(ONa) = C_6H_5N : NC_{10}H_6(ONa) + Na_2SO_4 + 2H_2O.$$

8. An acetic acid solution of dimethylaniline is added to a solution of the substance. A magnificent red colour is produced in a short time through the formation of dimethylaminoazobenzene sulphate.

$$C_6H_5N_2SO_4H + C_6H_5N(CH_3)_2.HOOC.CH_3 =$$
$$C_6H_5N : N.C_6H_4N(CH_3)_2.H_2SO_4 + CH_3COOH.$$

A sulphuric acid solution of *m*-phenylene diamine is added to the solution of the diazonium salt. The orange colour is due to diaminoazobenzene sulphate (Chrysoidine). Preparation 385.

$$C_6H_5N_2SO_4H + C_6H_4(NH_2)_2(H_2SO_4) =$$
$$C_6H_5N : NC_6H_3(NH_2)_2(H_2SO_4) + H_2SO_4.$$

9. A $\frac{1}{4}$ gm. at the most of the moist diazobenzene sulphate is allowed to dry spontaneously on filter paper in some safe place, and when dry exploded by kindling the paper.

For further information see "Aromatic Diazo Compounds" (Saunders).

**Reaction CLXXVIII. Action of Alkaline Reducing Agents on Aromatic Nitro Compounds.**—Azoxy, azo, and hydrazo compounds are formed.

The reducing agents employed, other than metals (see Reaction CLXX.) are sodium methoxide or ethoxide, alcoholic caustic soda or potash,

sodium amalgam, alkaline stannous chloride. The last reducing agent is usually employed for the isolation of azo compounds, while the others yield azoxy compounds, and, in some cases, hydrazo compounds.

$$4C_6H_5NO_2 + 3CH_3ONa \longrightarrow 2C_6H_5.N_2O.C_6H_5 + 3H.COONa + 3H_2O.$$

Better yields of azo and hydrazo compounds are sometimes obtained by reducing the azoxy compound in preference to the nitro compound. Certain hydrazo compounds, *e.g.*, hydrazo-naphthalenes, undergo the "benzidine conversion" (see p. 160) in alkaline as well as in neutral solution, so that the product finally isolated in the reduction is a diamino base. (J. C. S., 125, 1108.)

# CHAPTER XXVI

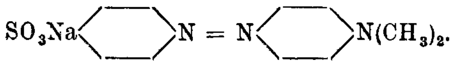
## DYES

### 1. Azo Dyes

THESE dyestuffs are formed by coupling diazonium compounds with phenols or aromatic bases. The characteristic group is $-N=N-$, and the general formula $X-N=N-Y$. Mono-azo dyes contain one $-N=N-$ group, while dis-azo dyes contain two, and so on. For the general laws of coupling, see Reaction CXXII. Mono-azo dyes are acid or basic in reaction, according to the nature of the auxochrome present (see p. 282). They are soluble in alkali and in conc. sulphuric acid if they contain a phenolic or sulphonic group. They are decomposed by conc. nitric acid and halogens. Reducing agents decompose them, with the formation of amines, a reaction which serves to determine their composition and constitution (see p. 365).

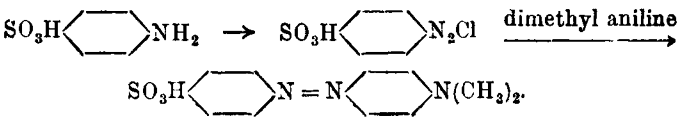
Special attention is directed to the test for completion of the "coupling" process on p. 492.

PREPARATION 383.—**Methyl Orange** (4-*Dimethylamino*-4′-*azobenzene*-*Na*-*sulphonate*).



$C_{14}H_{14}O_3N_3SNa$. 327.

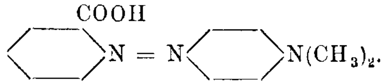
17·3 gms. of sulphanilic acid are dissolved in 150 c.cs. water containing 6 gms. sodium carbonate in solution. To this solution are added 7·2 gms. of sodium nitrite in 10% solution. The mixture is cooled by adding ice, and 25 c.cs. of hydrochloric acid in the form of a 15% solution (see p. 514), slowly added with stirring. 12·1 gms. of dimethylaniline are dissolved in an equal quantity of hydrochloric acid as above, and added to the diazonium compound. Caustic soda solution is then added till the solution is just alkaline. The methyl orange separates at once. A further yield may be obtained by adding common salt until solution is saturated. The dyestuff is filtered off, and is recrystallised from water.



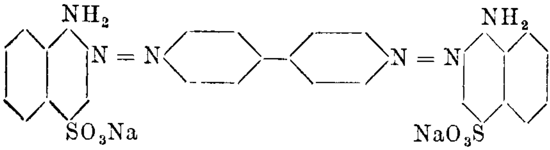
*Yield.*—Almost theoretical. (B., 10, 528.)

The sodium salt consists of yellow crystals dissolving in water to a yellow solution which turns red on addition of mineral acid. The dye is used as an indicator in acidimetry and alkalimetry.

If anthranilic acid is used in place of sulphanilic, the dyestuff formed is *Methyl Red*. (O. S., II., 47.)



PREPARATION 384.—**Congo Red.**



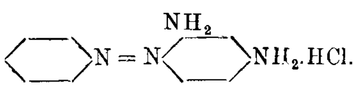
$C_{32}H_{23}O_6N_6S_2Na_2$. **697**

18·4 gms. benzidine are dissolved in 300 c.cs. of water and 20 c.cs. conc. hydrochloric acid, heat being applied, if necessary. Ice is added till the temperature is below 5°. 30 c.cs. conc. hydrochloric acid are then added, and about 14·4 gms. sodium nitrite in 10% solution until diazotisation is complete (see p. 372). 150 gms. sodium naphthionate are dissolved in as little water as possible. The diazonium solution is run into the sodium naphthionate, with stirring, and after ½ hour a solution of 35 gms. sodium carbonate is added gradually, so that during further stirring the solution is always alkaline. The contents of the beaker will appear brown at this stage. The whole is then slowly heated up to about 80° and common salt added to saturate the solution. After cooling, the reddish-brown Congo red is filtered off, washed with saturated common salt solution, and dried. Dyes cotton, direct from alkaline bath, red.

In order to obtain a good yield a large excess of sodium naphthionate is employed, the excess being recovered as the free acid on acidifying the mother liquor after filtering off the dyestuff. (B., 19, 1719.)

If *o*-tolidine is used in place of benzidine, the dyestuff formed is *Benzopurpurin 4B*. (D.R.P., 84893.)

PREPARATION 385.—**Chrysoidine Y** (2 : 4-*Diaminoazobenzene Hydrochloride*).



$C_{12}H_{13}N_4Cl$. 248·5.

9·3 gms. aniline are mixed with 100 c.cs. water. Ice is added and 30 c.cs. conc. hydrochloric acid. The solution is then diazotised by adding gradually about 7·2 gms. sodium nitrite in 10% solution (see p. 372). The solution should be kept below 5°.

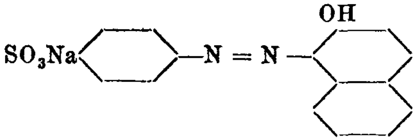
11 gms. *m*-phenylenediamine are dissolved in 200 c.cs. water, and made just acid with hydrochloric acid. The diazonium solution is then poured into the diamine solution, and the whole stirred for some time, until coupling is complete. Test (see p. 492).

The solution is heated to about 60°, and common salt added to saturate the solution. After standing till cold, the chrysoidine separates out as reddish-brown crystals, which are filtered off, washed with saturated common salt solution, and dried.

Dyes wool, silk, and tannin-mordanted-cotton orange.
(B., 10, 388.)

If *m*-tolylenediamine is used in place of *m*-phenylenediamine, the dyestuff formed is *Chrysoidine R.*

PREPARATION 386.—**Orange II.**

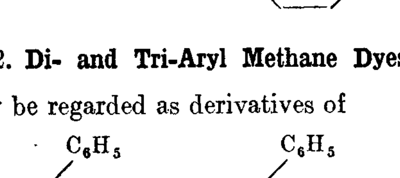


$C_{16}H_{11}O_4N_2SNa$. 350.

17·3 gms. sulphanilic acid are dissolved in water containing a little caustic soda. Ice is added to cool below 5°. 30 c.cs. hydrochloric acid are then added, and about 7·2 gms. sodium nitrite in 10% solution gradually run in until diazotisation is complete (see p. 372). The diazo compound usually separates out as fine needles, but these are not isolated. 14·4 gms. β-naphthol are dissolved in 15 c.cs. water, to which 4·5 gms. caustic soda have been added. This solution is made up to about 180 c.cs. by adding water. It is then cooled if necessary. The diazonium solution is carefully added, with stirring, until coupling is complete (see p. 492), the temperature not being allowed to rise above 8°. The mass should now give a slight alkaline reaction. After stirring for about an hour the dyestuff separates out, a little salt being added to complete the precipitation. The orange powder is filtered off and dried.

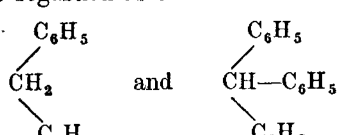
Dyes wool orange from an acid bath. (J. S. C. I., 6, 591.)

If α-naphthol is used in place of β-naphthol, the dyestuff formed is Orange I. (J. S. C. I., 6, 591.)



## 2. Di- and Tri-Aryl Methane Dyes

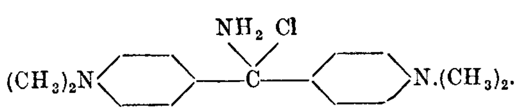
These dyes may be regarded as derivatives of



Diphenylmethane. Triphenylmethane.

The dyes are obtained from their amino, alkylamino and hydroxy derivatives, these groups being usually present in the *p*-position.

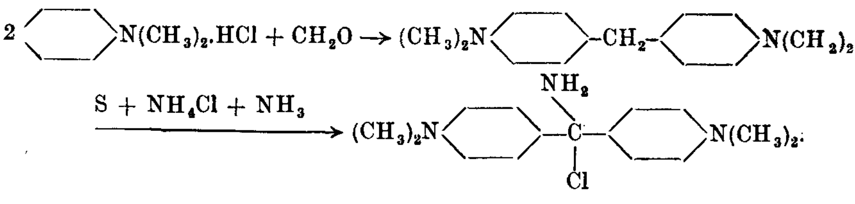
PREPARATION 387.—**Auramine.**



$C_{17}H_{22}N_3Cl$. 303·5.

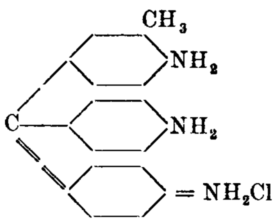
242 gms. pure dimethylaniline are mixed with 140 c.cs. water and 260 gms. conc. hydrochloric acid, and heated to 30°. 60 gms. 40% formaldehyde solution are then added, and the mixture heated to 85°, with stirring, for 5 hours. The base is then precipitated by adding 120 gms. sodium carbonate dissolved in a little water. The product, tetramethyl-diamino-diphenylmethane, is filtered after cooling to 20°, and washed with water. It is dried at 50°. The yield of this base is almost quantitative. 127 gms. diamino base, 32 gms. sulphur, 70 gms. ammonium chloride, and 1,000 gms. common salt are heated to 110° in an autoclave provided with stirrer and exit tube. The substances should be finely powdered and dried. The temperature is raised to 130° during 2 hours, and a rapid stream of *dry* ammonia passed through. At 140° a vigorous evolution of hydrogen sulphide begins, which lasts from 5—7 hours, according to the speed of the stream of ammonia. The temperature is raised to 145° during 5 hours, stirring being continued. The ammonia stream should pass at a speed of about 5 bubbles per second, and it is advisable to have a slight excess pressure of $\frac{1}{5}$ atm. measured by a manometer, which can be conveniently done by throttling the exit tube.

When the evolution of hydrogen sulphide has ceased, the contents of the autoclave are placed in a large basin and treated with 3 litres of water to dissolve out the salt. The dye is then filtered off, and dissolved in $1\frac{1}{2}$ litres of water at 60°. The solution is filtered, and a litre of saturated salt solution added, when the auramine comes down in glistening, golden leaflets. It is filtered and dried.




*Yield.*—Up to 175 gms. Dyes cotton mordanted with tannin or tartar emetic a pure yellow. (B., 33, 318.)

PREPARATION 388.—**Magenta** (*Fuchsine*).

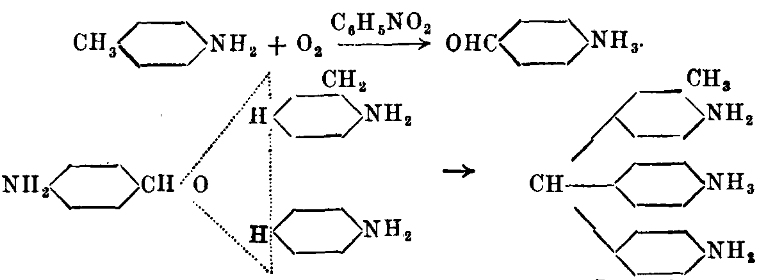



$C_{20}H_{20}N_3Cl$. 337·5.

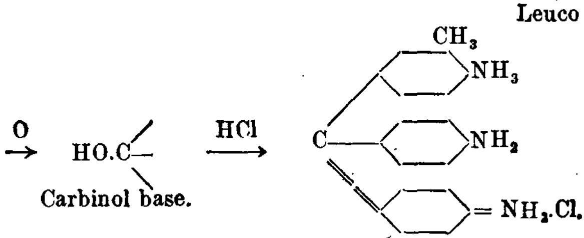
7 gms. aniline and 27 gms. commercial toluidine (containing 64% *ortho* and 36% *para*) are heated with 34 gms. conc. hydrochloric acid to 130° in a 250-c.c. flask. 3 gms. aniline, 13 gms. commercial toluidine, and

27·5 gms. nitrobenzene are then added. The flask is transferred to an oil bath at 100°, and 1·5 gms. iron powder dissolved in the minimum quantity of hydrochloric acid (2 mols.) slowly added. An air condenser is attached, and the temperature raised to 180°, and maintained at this temperature for about 5 hours. When a sample, withdrawn on a glass rod, solidifies on cooling, the action is finished. The mixture is then steam distilled to remove the nitrobenzene and excess amines. The melt is then poured into 250 c.cs. boiling water, with stirring, and 6 c.cs. conc. hydrochloric acid added slowly. As soon as an acid reaction is obtained, 13 gms. common salt are added, and the whole boiled for a few minutes. The aqueous solution (containing the hydrochlorides of aniline and toluidine) is poured off and the residue allowed to cool, when it solidifies to a green mass. This mass is broken up and extracted with 750 c.cs. boiling water containing 6 c.cs. conc. hydrochloric acid, which dissolves the magenta. The solution is filtered hot, and, after cooling to 60°, is again filtered. The magenta is then "salted out" with common salt, and after standing some time is filtered off and recrystallised from water containing a little hydrochloric acid.

The hydrochloride forms green, glistening crystals, giving a red solution in water. It dyes silk and wool bluish-red directly, and mordanted cotton.

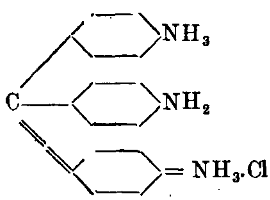



Leuco base.




Carbinol base.

Magenta.

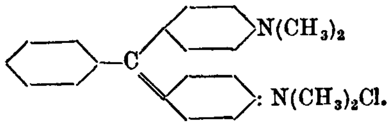



is also formed.

Pararosaniline chloride.

(J. S. C. I., 5, 163; 7, 118.)

PREPARATION 389.—**Malachite Green.**



**$C_{23}H_{25}N_2Cl$.** **364·5.**

*Method I.*—50 gms. dimethylaniline, 20 gms. of benzaldehyde and 20 gms. of pulverised anhydrous zinc chloride (see p. 509) are heated in a porcelain dish, with frequent stirring, on a water bath for 4 hours. The mass is then melted by the addition of hot water and transferred to a large flask, where it is steam distilled until no more dimethylaniline passes over. The leuco-base of the dye remains in a viscous form on the sides of the flask after cooling; the aqueous solution is decanted and the base washed a few times by decantation with cold water. The base is dissolved in boiling alcohol, the solution filtered hot, and the filtrate left overnight in an ice chest. Colourless crystals separate, which are collected and dried in air on filter paper. A second crop may be obtained by concentrating the mother liquor. If the base separates as an oil, instead of crystals, more alcohol should be added, and heat applied until the oil redissolves.

A small portion of the leuco-base is weighed, dried at 100°, and weighed again in order to determine its moisture content. The equivalent of 10 parts by weight of the anhydrous base is dissolved by heating with a quantity of dilute hydrochloric acid, corresponding to 2·7 parts by weight of hydrogen chloride. The colourless solution of the leuco-base is diluted in a large beaker with 800 parts of water, and 10 parts of 40% acetic acid added. The solution is cooled to about 0° by the addition of lumps of ice, and a freshly prepared lead dioxide paste (for preparation and estimation, see p. 507), corresponding to 7·5 parts $PbO_2$, added gradually during the course of 10 minutes, the mixture being stirred and cooled during the addition. Stirring is continued for 2 hours, after which the unchanged lead peroxide is filtered off, and the lead in the filtrate precipitated by the addition of 10 parts of sodium sulphate dissolved in 50 parts of water. Lead sulphate is filtered off, the filtrate is heated to boiling, and 15 gms. of sodium chloride added for each 100 c.cs. of dye solution; while still hot, 8 parts of zinc chloride, dissolved in a small quantity of water, are also added. On cooling, the zinc chloride double salt of the dye is filtered off, washed with saturated sodium chloride solution, and dried on a porous plate. If the mother liquors are coloured, owing to some of the dye still remaining in solution, a further crop may be obtained by adding more sodium chloride and zinc chloride.

$$C_6H_5CHO + 2C_6H_5N(CH_3)_2 \rightarrow \underset{\text{(Leuco-base)}}{C_6H_5CH\{C_6H_4N(CH_3)_2\}_2} + H_2O$$

$$\downarrow O$$

$$\underset{\text{Malachite green hydrochloride.}}{C_6H_5{-}C{\begin{cases} C_6H_4N(CH_3)_2 \\ C_6H_4 = N(CH_3)_2Cl \end{cases}}} + H_2O \xleftarrow{\text{HCl}} \underset{\text{(Carbinol base.)}}{C_6H_5C(OH)\{C_6H_4N(CH_3)_2\}_2}$$

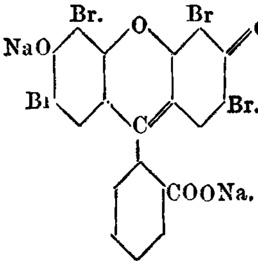
The formula of the zinc chloride double salt is $2C_{23}H_{25}N_2Cl, 2ZnCl_2, H_2O$.

Brass yellow prismatic needles; soluble in hot water to a bluish-green solution; dyes silk, wool, jute and leather, a bluish-green directly, and cotton which has been previously mordanted with tannin and tartar emetic.

*Method II.*—50 gms. dimethylaniline, 20 gms. benzaldehyde, and 45 gms. of conc. hydrochloric acid are placed in a flask fitted to a reflux condenser, and the mixture heated at 100° for 24 hours. The product is then made alkaline with caustic soda, and steam distilled to remove traces of benzaldehyde and dimethylaniline. After this the procedure is the same as in Method I. (J. S. C. I., 6, 433.)

### 3. Pyrone or Phthalein Dyes

PREPARATION 390.—**Eosin** (*Tetrabromofluorescein*).

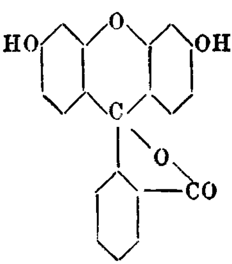


$C_{20}H_6O_5Br_4Na_2$. 692.

Into a mixture of 15 gms. of fluorescein and 60 gms. of alcohol (about 95%), contained in a flask, are added with frequent shaking 11 c.cs. of bromine, drop by drop, from a burette. When half the bromine has been added the dibromide which is then formed is in solution; on further addition of bromine the tetrabromide separates out in the form of brick-red leaflets. After all the bromine has been added, the mixture is allowed to stand for 2 hours. The precipitate is filtered off, washed first with alcohol, then with water, and converted into the sodium salt by mixing with a little hot water, carefully neutralising with caustic soda (avoiding excess), and evaporating to dryness on a water bath.

Bluish-red crystals or brownish-red powder. In water, bluish-red solution; dilute solution has green fluorescence. In alcohol, easily soluble, with bluish-red colour and yellowish-green fluorescence. Dyes wool and silk yellowish-red. (J. S. C. I., 12, 513.)

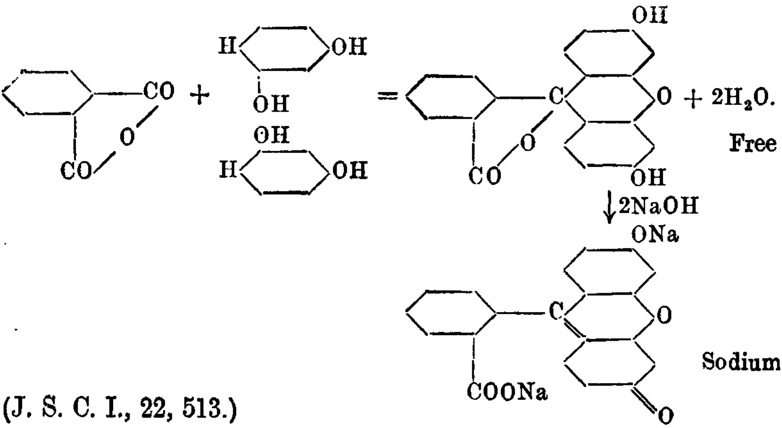
PREPARATION 391.—**Fluorescein.**



$C_{20}H_{12}O_5$. 332.

A mixture of 15 gms. of phthalic anhydride and 22 gms. of resorcinol is ground in a mortar. It is then transferred to a nickel or cast-iron vessel, and heated in an oil bath to 180°. At this temperature 7 gms. of powdered fused zinc chloride (see p. 509) are added, with stirring, during the course of 10 minutes. The temperature is raised to 210°, and maintained at this point until the liquid, which gradually thickens, becomes solid, for which 1—2 hours are required. The cold melt is removed from the vessel with a knife or chisel, powdered, and boiled 10 minutes with 200 c.cs. of water and 10 c.cs. of conc. hydrochloric acid. This treatment causes the solution of zinc oxide and basic zinc chloride. The fluorescein is filtered off, washed with water until the filtrate no longer shows an acid reaction; it is dried on a water bath.

*Yield.*—Almost theoretical (32 gms.). Red powder; slightly soluble in water; soluble in alcohol; soluble in alkali with intense green fluorescence; dyes animal fibres a fast yellow.



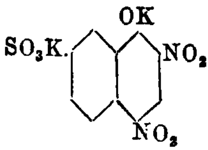
**Free acid.**

**Sodium salt.**

(J. S. C. I., 22, 513.)

## 4. Nitro Dyes

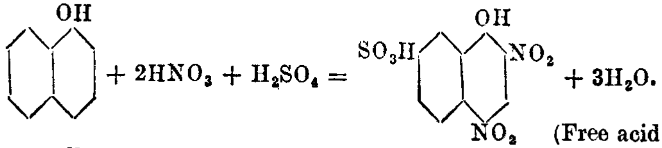
PREPARATION 392.—**Naphthol Yellow S.** (2 : 4-*Dinitro*-1-*naphthol*-7-*sulphonic acid*) (**K Salt**).



$C_{10}H_4O_8N_2SK_2$. **390.**

100 gms. of conc. sulphuric acid are warmed to 100° in a small flask, 50 gms. of powdered $\alpha$-naphthol are added in one instalment. The mixture is raised to 120° by heating in an oil or sand bath and maintained at this temperature for 3—4 hours. The sulphonation mixture is then poured into 600 c.cs. of water, which are stirred mechanically. When the temperature of the mixture falls to 30° it is poured into a mixture of 23 gms. of conc. nitric acid and 8 c.cs. of water, which is well stirred mechanically; the temperature is kept below 35° by cooling in water, if necessary. A further 21 gms. of conc. nitric acid are added at such a

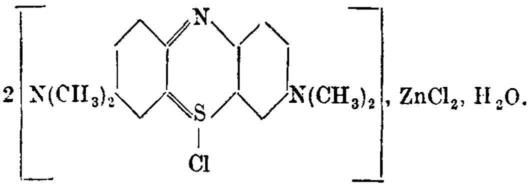
rate that the temperature does not rise above 40°. The nitration mixture is filtered through woollen cloth and washed free from acid with 10% sodium chloride solution. The drained precipitate is stirred with 200 c.cs. of hot water at 80°, solid sodium carbonate added until neutral, and the dyestuff precipitated by adding 20 gms. potassium chloride.




Orange-yellow powder; dyes wool and silk from an acid bath. (A., 152, 299.)

## 5. Thiazine Dyes

PREPARATION 393.—**Methylene Blue** (*Tetramethylthionine Chloride*) (**Hydrated zinc double chloride**).




*Nitrosodimethylaniline.*—16 gms. of dimethylaniline are dissolved in 53 gms. of conc. hydrochloric acid (30%) and 100 gms. ice added. 10·5 gms. of sodium nitrite previously dissolved in 40 c.cs. water are then slowly run in from a dropping funnel, the solution being agitated during the addition. The temperature must be kept at 0°—5° by the addition of ice, when necessary. When the nitrite is added, the agitation is stopped, and a test for the presence of free nitrous acid applied. A sample of the liquor is withdrawn, diluted with 3 times its volume of water, and tested with starch-iodide paper. If test does not indicate free nitrous acid, more nitrite must be added until a positive indication is obtained. The solution should be acid to Congo paper, and of a yellow colour; if not acid it is somewhat green. After the addition of all the nitrite the mixture is allowed to stand for 2 hours, and at the end of this time it should just give a slight indication of free nitrous acid. The greater part of the nitrosodimethylaniline hydrochloride separates out as yellow crystals.

p-*Aminodimethylaniline.*—The above mixture is well agitated, 100 c.cs. of water and 70 gms. of conc. hydrochloric acid added; this is followed by 20 gms. iron filings, and sufficient ice added from time to time to keep the temperature below 30°. The reduction is complete when a drop spotted on filter paper is quite colourless. The liquor, which is generally acid, is treated with lime-paste until it is only faintly acid to Congo paper; the neutralisation is completed by the addition of chalk until frothing stops. The residue of iron and chalk is filtered off and washed, the washings being added to the filtrate.

*Thiosulphonic Acid and Dye.*—Before entering on this stage of the preparation the following solutions are prepared :—

*Sodium I.*—33·5 gms. sodium thiosulphate in 40 c.cs. water.

*Solution II.*—26·4 gms. sodium bichromate in 40 c.cs. water.

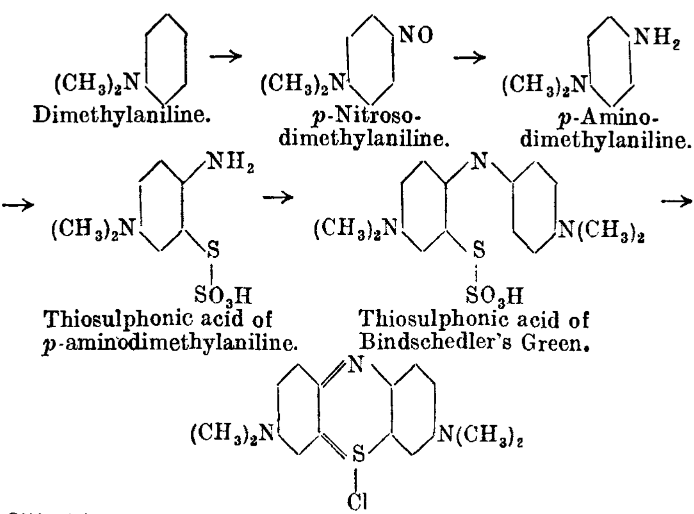
*Solution III.*—14 gms. dimethylaniline in 24 gms. conc. hydrochloric acid.

*Solution IV.*—26·4 gms. sodium bichromate in 40 c.cs. water.

*Solution V.*—1·5 gms. copper sulphate in 20 c.cs. water.

The clear neutral solution of *p*-aminodimethylaniline is vigorously agitated. Solution I. is added all at once, and immediately following it Solution II. during the course of 2 minutes. After an interval of 2 minutes Solution III. is added all at once, and immediately following it Solution IV. during the course of 2 minutes. Agitation is continued for 7 minutes before Solution V. is added. The mixture is then transferred to a large vessel and heated ; it soon assumes a bronze appearance, and much frothing takes place. Heat is withdrawn until the froth settles ; when this occurs, the mixture is heated up again and filtered almost boiling. The black precipitate of chromium hydroxide is washed with boiling water until the filtrate is only faintly coloured. The total filtrate is heated almost to boiling, then treated with 150 gms. common salt, 40 gms. of 50% zinc chloride solution and 10 gms. conc. hydrochloric acid. On cooling, the double zinc salt of methylene blue separates out as a coppery powder, which is filtered off and washed with a little 10% brine solution ; it is dried at a temperature not exceeding 50°, a yield of about 30 gms. being obtained.

If " zinc-free " methylene blue is desired, the filtrate from the chromium hydroxide is heated to 80°, 15 gms. of common salt added for each 100 c.cs. of solution, also 10 c.cs. of conc. hydrochloric acid. On cooling, the " zinc-free " methylene blue separates in fine crystals.




(A., 251, 1.) Methylene Blue.

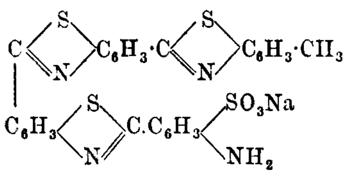
Methylene blue is of a very pure shade, and is much used for dyeing tannined cotton; the "zinc-free" dye is used for medicinal purposes, and also for the production of discharge effects in silk printing.

PREPARATION 394.—**Methylene Green** (*Nitromethylene Blue*).

30 gms. methylene blue (Zn salt) are made into a paste with 35 c.cs. water and 16 gms. of 60% nitric acid; to this are added at 25°, 3·5 gms. of sodium nitrite dissolved in the minimum quantity of water. The temperature is raised slowly to 50° (rate 1° per minute) with good agitation, and kept there for 2 hours. 160 gms. of saturated brine are then added, and the precipitate filtered off after 12 hours. The product is purified by dissolving in 800 c.cs. water at 60°, filtering to remove residue, and reprecipitating the dye with 105 gms. common salt along with 35 gms. of 50% zinc chloride solution. After standing for 12 hours, the dye is filtered off, pressed, and dried at 45°.

*Yield.*—About 25 gms. Used in conjunction with iron-mordanted logwood, or with tin phosphate for dyeing black on silk, also for cotton and calico printing. (E.P., 8992 (1886).)

PREPARATION 395.—**Primuline.**




$C_{28}H_{17}O_3N_4S_4Na$. **608.**

20 gms. *p*-toluidine and 14 gms. sulphur are well mixed together and heated in a jar in an oil bath to 250°. The mass turns yellow, and the reaction is finished when no more $H_2S$ is evolved.

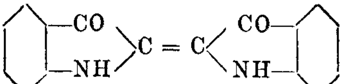
The mass, after cooling, is powdered and heated with 4 times its weight of fuming sulphuric acid (30% $SO_3$) to 70°—80° for a few minutes until a sample dissolves in caustic soda. The sulphonation mixture is poured into ice-water, and the sulphonic acid of the primuline base which is precipitated filtered and washed free of acid.

The paste is stirred up with dilute ammonia until alkaline, filtered and washed with cold water. The residue is the ammonium salt of dehydro-thio-*p*-toluidinesulphonic acid (p. 326), and the filtrate contains the primuline. The filtrate is saturated with common salt, when the primuline separates out and is filtered and dried.

Dyes cotton direct from alkaline or neutral bath primrose-yellow (see Preparation 302). (D.R.P., 56606.)

## 6. Indigoid Dyes

PREPARATION 396.—**Indigo.**

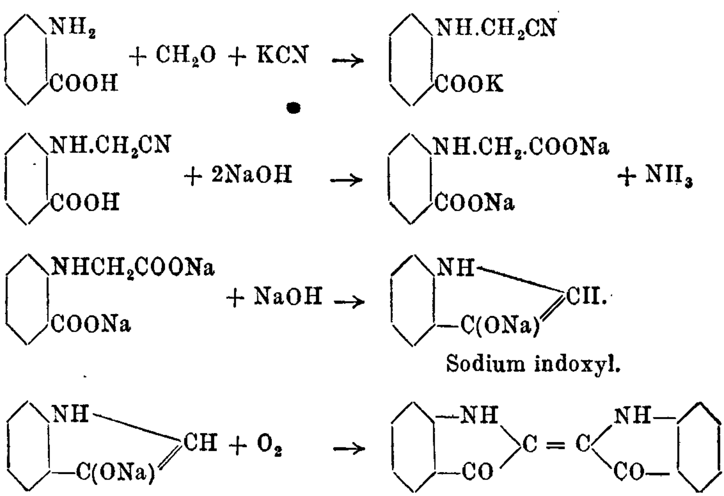



$C_{16}H_{10}O_2N_2$. 262.

14 gms. anthranilic acid are suspended in 50 c.cs. benzene. 7 gms. finely powdered potassium cyanide are added, and after shaking, 7·5 c.cs. of 40% formaldehyde. The temperature rises, and the potassium salt of ω-cyanomethyl anthranilic acid is formed in the aqueous liquid.

The benzene is removed, and 20 c.cs. of 40% caustic soda solution are added. The mixture is carefully heated over a wire gauze until ammonia begins to be evolved. After the reaction has subsided, heating is continued until all the ammonia is driven off, water being added, if necessary, to prevent the contents of the flask becoming solid. The mixture, when cold, is carefully neutralised with conc. hydrochloric acid (using phenolphthalein as indicator), and then acidified with about 15 c.cs. of glacial acetic acid. The yellowish-white precipitate of phenyl-glycine-*o*-carboxylic acid is filtered off, washed with water, and dried on a porous plate.

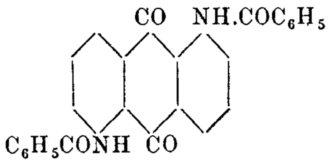
10 parts of phenylglycine-*o*-carboxylic acid, or the corresponding amount of the sodium potassium salt, are added to a solution of 10—12 parts of pure caustic soda in 4—6 parts of water. The mixture is then quickly evaporated, being stirred continuously until dry. It is powdered, and added to 8—14 parts of solid paraffin (M.P. about 160° F.). The mixture is heated to 250°—270°, and stirred with the thermometer, steam being evolved. The end of the reaction is indicated by the strong yellow colour of the fusion. The homogeneous paste is cooled, and boiled with water containing a little sodium " hydrosulphite " to prevent oxidation. The liquid is filtered from paraffin, and oxidised by passing air, when indigo is precipitated as a dark blue powder.




Indigo dissolves in most alkaline reducing agents to give a colourless leuco-compound. Cotton, wool and silk are dyed by soaking in the leuco-compound and exposing to air. (D.R.P., 125916.)

## 7. Anthraquinone Dyes

PREPARATION 397.—**Algol Yellow R** (1 : 5-*Di-(benzoylamino)-anthraquinone*).



$C_{28}H_{18}O_4N_2$. 446.

7 gms. of 1 : 5-dinitroanthraquinone (Preparation 234) are added to a solution of 35 gms. sodium sulphide ($Na_2S.9H_2O$) in 200 c.cs. water, and heated gradually to boiling. The mass becomes dark blue and thick, owing to the separation of sulphur and diamino-anthraquinone. The precipitate is filtered off and extra yield recovered by adding common salt to the filtrate.

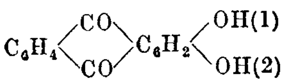
The diamino compound is then extracted from the precipitate by boiling up with alcohol and filtering from sulphur. The diamine is precipitated from the alcoholic solution by adding water. It is filtered and dried on the water bath.

Scarlet red powder; M.P. 262°. J. C. S., 1932, 83.

*Benzoylation.*—1 gm. of the diamino compound is treated with 4 gms. benzoyl chloride and 10 gms. dimethylaniline and boiled for 1 hour, when the benzoyl derivative separates out as a yellow-brown powder. The unchanged base and the dimethylaniline are extracted with dilute hydrochloric acid. The product is then filtered.

Yellowish powder; M.P. 234°.

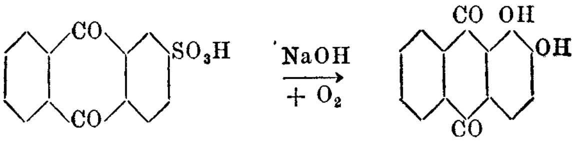
PREPARATION 398.—**Alizarin** (1 : 2-*Dihydroxyanthraquinone*).



$C_{14}H_8O_4$. 240.

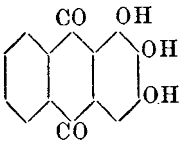
100 gms. 100% β-anthraquinone sulphonate "silver salt" (see p. 315) are mixed with 260 gms. 100% caustic soda, 28 gms. sodium chlorate, and sufficient water to make volume up to 670 c.cs. The mixture is placed in an autoclave and heated up to 185° with continuous stirring, the pressure attaining 5—6 atms. After 48 hours, the melt is allowed to cool, and the following test applied; 2 c.cs. of the melt are treated with sufficient conc. hydrochloric acid to precipitate the alizarin. The filtrate is then extracted twice with a little ether to remove traces of alizarin. The liquid is now diluted to 15 c.cs., and the fluorescence, which is due to unchanged silver salt and the monohydroxysulphonic acid, observed. If the reaction is complete, only a very faint fluorescence should develop. If the reaction is not complete, the mixture is heated up again in the autoclave to 190° for 24 hours. It is then diluted with 2 litres of water, and the alizarin precipitated *at the boil* with 50% sulphuric acid. It

is cooled to 50°, filtered and washed. It is not dried, as when once dry it no longer dyes properly.



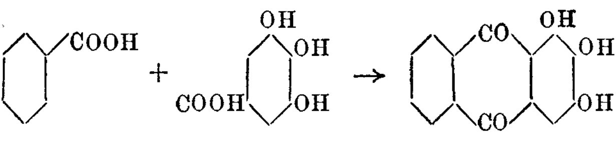
*Yield.*—About 70 gms. M.P. 289°. A polygenetic dyestuff, *i.e.*, dyes mordanted cotton various colours, depending on the mordant used, *e.g.*, iron oxide gives a violet colour, alumina a red colour, chromium a brown colour, etc. (J. S. C. I., 2, 213 ; E.P., 1948 (1869).)

PREPARATION 399.—**Anthragallol** (1 : 2 : 3-*Trihydroxyanthraquinone*).



$C_{14}H_8O_5$. 256.

36 gms. pure benzoic acid are dissolved in 300 gms. sulphuric acid (monohydrate, p. 309) in a glass or porcelain beaker with good stirring. The mixture is heated slowly to 90°, at which temperature 50 gms. pure, dry gallic acid * (dried at 110°) are added in small portions during an hour. The temperature is then raised to 118°, and kept there for 6 hours, after which the melt is allowed to drop cautiously into a litre of boiling water, with continuous stirring. The product is filtered boiling through a hot filter, and the dye well washed with hot water. The excess benzoic acid crystallises out in the mother liquor.



*Yield.*—70—80% theoretical (70—80 gms.). Dyes wool brown with chrome mordants, chromium fluoride giving the best shades. (J. S. C. I., 3, 141.)

* Good quality gallic acid may be obtained by hydrolysing tannin with 40% caustic soda solution at 70° with the addition of a little sodium bisulphite to protect the acid from oxidation. The gallic acid is then precipitated by conc. hydrochloric acid and crystallised from water. (*Note.*—Sulphuric acid must not be used.)

# CHAPTER XXVII

## DRUGS

PREPARATION 400.—**Chloral Formamide** [1-*Formylamino*-2 : 2 : 2- *trichloroethanol*].

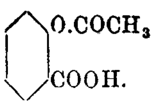
$CCl_3.CH(OH)NH.CHO$.  $C_3H_4O_2NCl_3$.  192·5.

74 gms. freshly distilled chloral are added, with stirring, to 22·5 gms. cooled formamide (see Preparation 268). Much heat is evolved, and the mixture sets on cooling to a crystalline mass of chloral formamide. It is purified by recrystallisation from dilute alcohol, the solution not being heated above 48° (see below).

$$CCl_3CHO + HCONH_2 \longrightarrow CCl_3CH(OH).NH.CHO.$$

Colourless crystals; M.P. 114°—115°; a hypnotic; above 48°, is reconverted to chloral and formamide. (D.R.P., 50586; E.P., 7391 (1886).)

PREPARATION 401.—**Acetylsalicylic Acid** (*Aspirin*).



$C_9H_8O_4$.  **180.**

100 gms. acetyl chloride in 25 gms. glacial acetic acid are added to 69 gms. salicylic acid in a retort. The retort is gently heated until the reaction commences, when heating is discontinued. Hydrochloric acid is evolved, and acetyl chloride commences to pass over. When the reaction slackens, the temperature is raised gradually to 60°, and when the action has ceased, to 70°, to remove acetyl chloride as far as possible. This can be much facilitated by a slight reduction of pressure. When the distillation has ceased the contents of the retort are poured into an enamelled basin and allowed to crystallise. The crystals are then filtered off, washed with water, and dried at 30°—40°. They are recrystallised by dissolving in ethyl alcohol at about 40°, and throwing out of solution by the addition of cold water.

$$C_6H_4\left\langle\begin{matrix}OH & [1]\\ COOH & [2]\end{matrix}\right. \longrightarrow C_6H_4\left\langle\begin{matrix}OCOCH_3 & [1]\\ COOH & [2]\end{matrix}\right.$$

Rhombic plates; M.P., which varies according to rate of heating, is given by British Pharmacopœia as 134°—135°; should give no violet coloration with ferric chloride; an important analgesic and antipyretic. (Bl., 17, 186.)

PREPARATION 402.—**Chloramine-T.**

$$CH_3.C_6H_4SO_2N(Na)Cl + H_2O. \qquad C_7H_9O_3NClSNa. \qquad 245{\cdot}5.$$

*p*-Toluene-sulphonyl chloride (see Preparation 287) is treated with 4 times its weight of dilute ammonia solution, and stirred for several hours, until all the powdered sulphonyl chloride is converted into the crystalline sulphonamide. A little of the mixture is filtered, and the crystals boiled with water. When no acidity is developed the reaction is complete. The crystals are then filtered off, washed with a little water, and recrystallised from a small quantity of water. Needles; M.P. 64°.

$$CH_3C_6H_4SO_2Cl \longrightarrow CH_3C_6H_4SO_2NH_2.$$

171 parts of *p*-sulphonamide are treated with 525 parts of a 2N solution of sodium hypochlorite (see p. 512) containing 40 parts NaOH. A white precipitate is immediately formed, which, on heating and subsequent cooling, deposits crystals of Chloramine-T, which are washed with brine and recrystallised from water.

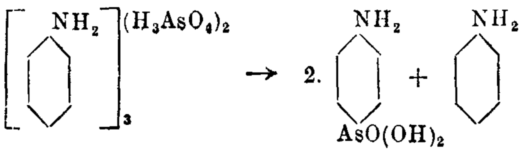
$$CH_3C_6H_4SO_2NH_2 + NaOCl \longrightarrow CH_3C_6H_4SO_2N(Na)Cl.$$

Colourless needles; powerful disinfectant. (J. S. C. I., 37, 288.)

PREPARATION 403.—**Arsanilic Acid** (p-*Aminophenylarsinic acid*).


$C_6H_8O_3NAs.$ 217.

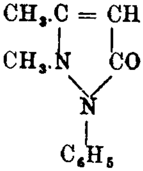
Syrupy arsenic acid (85%; D. 2·00) is prepared by dissolving 36 gms. of commercial arsenic acid in 16 c.cs. water (check specific gravity). This is placed in an evaporating dish, and 40 c.cs. aniline added in 10 c.c. portions, the solid formed being broken up with a glass rod. The aniline arsenate is then transferred to a round-bottomed flask and an additional 40 c.cs. aniline added, and the mixture heated on an oil bath at 170°—175° until completely melted. The melt is then maintained at 155°—160° for 5 hours with continuous stirring, and poured into 35 c.cs. water. The flask is washed out with a portion of previously prepared solution of 17 gms. caustic soda in 70 c.cs. water, and the washings added with the remainder of the alkali to the reaction mixture, with stirring. The mixture is cooled and separates into two dark coloured layers, the top layer consisting chiefly of aniline, and the bottom of an aqueous solution of sodium arsanilate. The two layers are carefully separated in a funnel, warming if necessary, to keep the arsanilate in solution. The aqueous solution is then boiled with decolorising carbon and filtered. The filtrate is treated with conc. hydrochloric acid until it is just acid to Congo Red, and allowed to stand for 24 hours, occasionally scratching the sides of the vessel, if necessary, with a glass rod to induce crystallisation. The crystals are then filtered off, and recrystallised from about 125 c.cs. of water.



*Cf.* Sulphanilic acid. *Yield.*—12 gms.

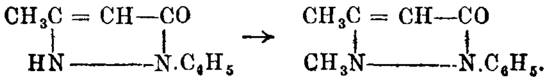
The sodium salt, $NH_2.C_6H_4.AsO(OH)(ONa) + 5H_2O$, prepared by neutralising 1 mol. of the acid with 1 mol. caustic soda, is known as "Atoxyl." (Am. Soc., 41, 451 ; O. S., III., 13.)

PREPARATION 404.—**Antipyrine, Phenazone** (1-*Phenyl*-2 : 3-*dimethyl*-5-*pyrazolone*).



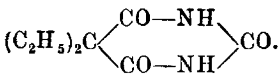
$C_{11}H_{12}ON_2$. **188.**

Phenylmethyl pyrazolone (see Preparation 252) is methylated with a methyl alcoholic solution of methyl chloride or bromide at 90°—100°, a slight excess of methylating agent being employed. The methylation can be conveniently carried out in an autoclave fitted with an agitator. The alcohol is distilled off, and the reaction product dissolved in water made slightly alkaline with caustic soda. The antipyrine is then extracted with benzene, and crystallised from benzene, and finally from water, animal charcoal being used to decolorise.



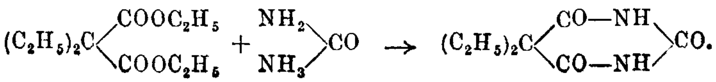
White crystalline scales ; M.P. 113° ; odourless ; possesses bitter taste ; a valuable analgesic and antipyretic. (D.R.P., 69883, 26429.)

PREPARATION 405.—**Veronal, Barbitone** (*Diethylmalonyl urea*, 5 : 5-*diethyl-barbituric acid*).



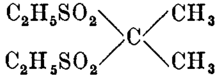
$C_8H_{12}N_2O_3$. 184.

16 gms. sodium are dissolved in 300 gms. absolute alcohol. To the cooled solution are added 20 gms. dry urea and 50 gms. diethyl malonic ester (see Reaction XLIV. (*a*) ). The mixture is heated in an autoclave for 4—5 hours at 100°—110°. On cooling, the sodium salt of diethyl barbituric acid separates, is filtered off, dissolved in water, and the free acid precipitated by the addition of hydrochloric acid. The acid is filtered and recrystallised from water, using animal charcoal if necessary.



Colourless crystals; M.P. 191°; an important hypnotic. (D.R.P., 146496; Am. Soc., 40, 725.)

PREPARATION 406.—**Sulphonal** (*Diethylsulphonedimethylmethane*).



$C_7H_{16}O_4S_2$. 228.

1. *Acetone Ethyl Mercaptol.*—50 gms. ethyl mercaptan (see Preparation 306) are added to 20 gms. acetone and 6 gms. anhydrous calcium chloride. Dry hydrochloric acid gas is passed in, the temperature being kept below 25° by external cooling. When saturated with acid the mixture is allowed to stand overnight, and washed with water. The layer of mercaptol is separated and dried over calcium chloride, and fractionally distilled. Unchanged ethyl mercaptan passes over first, and then the mercaptol at 190°.

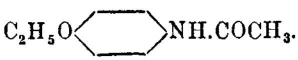
$$2C_2H_5SH + OC.(CH_3)_2 \rightarrow (C_2H_5S)_2C(CH_3)_2 + H_2O.$$

2. *Sulphonal.*—33 gms. acetone ethyl mercaptol are added with brisk agitation to 1 litre of 5% potassium permanganate solution. The mixture gradually warms up as oxidation proceeds. About 85 gms. solid permanganate are gradually added at intervals. Stirring is continued until the permanganate is reduced, when the solution is boiled and decolorised with animal charcoal. Sulphonal separates out on cooling, is filtered, and recrystallised from aqueous alcohol.

$$(C_2H_5S)_2.C(CH_3)_2 \rightarrow (C_2H_5SO_2)_2.C.(CH_3)_2.$$

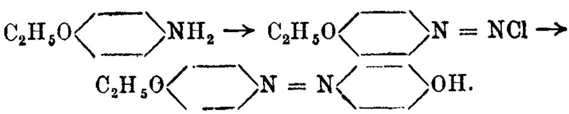
Colourless, odourless, tasteless, prismatic crystals; M.P. 125·5°; a hypnotic. (B., 19, 280.)

PREPARATION 407.—**Phenacetin** (*Aceto*-p-*phenetidine*).



$C_{10}H_{13}O_2N$. **179.**

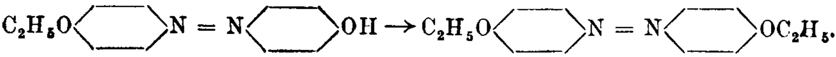
(1) 13·7 gms. *p*-phenetidine (see Preparation 368) are dissolved in 200 c.cs. water and 37·5 gms. 20% hydrochloric acid, and diazotised below 6° with 6·3 gms. sodium nitrite. The diazonium solution is then run into a solution of 9·5 gms. phenol in 350 c.cs. of 2% sodium carbonate solution. The azo compound separates out in about 1 hour, and is filtered off and dried.



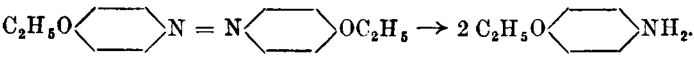
*Yield.*—Theoretical. M.P. 104·5°.

(2) 24 gms. of the azo compound are dissolved in 100 c.cs. alcohol and 4 gms. caustic soda. The solution is then placed in an enamel-lined autoclave, 7 gms. ethyl chloride are added, and the whole is heated under

pressure for 5—6 hours at 90°—100°. On cooling, the diethoxy azo compound separates, and is filtered off (M.P. 156°).

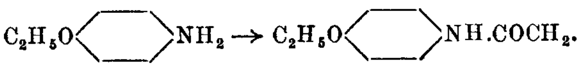


(3) 10 gms. of the diethoxy azo compound are mixed with 50 gms. 20% hydrochloric acid, and 6 gms. of granulated tin are added. When all has gone into solution, caustic soda solution is added to make alkaline, and the *p*-phenetidine distilled over by superheated steam at 160°—180°.



2 mols. of *p*-phenetidine are thus prepared from the initial 1 mol. of *p*-phenetidine. (D.R.P., 48453.) See also U.S.P., 1890430.

(4) Equal weights of distilled *p*-phenetidine and glacial acetic acid are heated under a reflux with the addition of a little fused sodium acetate until no free base remains (diazotise and test with alkaline $\beta$-naphthol). The excess acetic acid is removed by distillation *in vacuo*, and the residue dissolved in boiling water to which animal charcoal is added, and after cooling and filtering, phenacetin separates out. It is filtered, washed, and recrystallised from water or 60% alcohol, a little sulphur dioxide solution being added to prevent oxidation.



White glistening scales; M.P. 134°; a very important analgesic and antipyretic. (D.R.P., 139568.)

# CHAPTER XXVIII

## ELECTROLYTIC PREPARATIONS

### PREPARATION 408.—**Benzaldehyde.**

$C_6H_5.CHO$. $C_7H_6O$. **106.**

The apparatus for this preparation consists of a narrow glass beaker, or a wide-mouthed bottle. The beaker is corked, and an efficient glass stirrer passing through the centre is attached to a small turbine or motor. Four electrodes are fixed in position so that they are clear of the stirrer. Two anodes, each of sheet platinum of about 1 sq. dcm. surface, are placed diametrically opposite one another, while the two cathodes, spirals of platinum wire and each of 2 cms. surface, are placed between them near the sides of the beaker. 50 gms. toluene, 200 c.cs. of 10% sulphuric acid and 250 c.cs. of acetone are placed in the cell, which is surrounded by cold water. The current density should be 1·5—2 amperes, the E.M.F. 5—6 volts, and the temperature at 15°—20°. The stirring must be vigorous to keep the mixture in a thorough emulsion.

From the equation

$$C_6H_5.CH_3 + 2O = C_6H_5.CHO + H_2O.$$

50 gms. of toluene require 58 ampere hours, but in order to ensure complete oxidation 65 ampere hours should be passed. The contents are then transferred to a flask, and made slightly alkaline with sodium carbonate. The acetone is removed by distillation, and the residue steam distilled, when benzaldehyde and unchanged toluene pass over. Benzaldehyde is separated as its bisulphite compound, formed by shaking up with sodium bisulphite, allowing to stand to crystallise and filtering. Dilute caustic soda is then added, the benzaldehyde separated by steam distillation, dried, and redistilled.

*Yield.*—7—8 gms. (see p. 226). The procedure for *o*- and *p*-xylene is similar. (Am. Soc., 22, 723.)

### PREPARATION 409.—**Iodoform** (*Triiodomethane*).

$CHI_3$. 394.

20 gms. of anhydrous sodium *carbonate* and 20 gms. (8 mols.) of potassium iodide are dissolved in 20 c.cs. of water, 50 c.cs. (excess) of absolute alcohol added, and the whole poured into a beaker. The anode is a sheet of platinum foil, 8 by 10 cms., the cathode of platinum wire wound into a spiral of 1 cm. diameter.

The solution is warmed to 60°—70°, and a current of 3 amperes per sq. dcm., counting both sides of the anode, is passed through the solution,

while carbon dioxide is bubbled into the liquid to neutralise the caustic potash formed. After 1 hour the iodoform which has separated is filtered off and washed with cold water.

$$2KI + H_2O + CO_2 \rightarrow K_2CO_3 + H_2 + I_2.$$

$$CH_3CH_2OH \xrightarrow{I_2} CH_3CHO \xrightarrow{3I_2} CI_3CHO \rightarrow CHI_3.$$

*Yield.*—75% theoretical. Yellow crystals; insoluble in water; soluble in alcohol and ether; volatile in steam; M.P. 119°. (C., 1897, II., 695.)

PREPARATION 410.—**Methyl Alcohol.**

$$CH_3OH. \qquad CH_4O. \qquad 32.$$

A solution in 500 c.cs. water is made from 110 gms. potassium acetate, 26 gms. potassium carbonate and 28 gms. potassium bicarbonate, and poured into a lead cell or glass beaker, which need contain no anode chamber. The beaker should be placed in a basin of cold water, and the cathode should take the form of a thin lead pipe, with a copper connection soldered to it, wound in the form of a coil, and placed close to the inner walls of the beaker. Through this pipe a supply of cold water is run, so that the temperature is maintained at 25°—30° during the electrolysis. The anode is of platinum, and should be so arranged that it can be rotated. The current density is 20—25 amperes per sq. dcm., and the E.M.F. 7—8 volts.

As the electrolysis proceeds, acetic acid is dropped in at such a speed that the solution does not become acid. When 50—60 ampere hours have passed the electrolysis is stopped. The contents of the cell are then distilled to remove the methyl alcohol, and some formaldehyde, which is also produced. The alcohol is dried and redistilled in the usual way.

$$CH_3COO^+ + OH' \rightarrow CH_3OH + CO_2$$

*Yield.*—50—60% theoretical (see p. 213). (A., 323, 304.)

PREPARATION 411.—*p*-**Phenylenediamine.**

$$H_2N.C_6H_4.NH_2. \qquad C_6H_8N_2. \qquad 108.$$

20 gms. *p*-nitroaniline are dissolved in 150 c.cs. of alcohol, and to this is added a solution of 5 gms. sodium acetate in 100 c.cs. hot water. This mixture is then placed in a beaker, which acts as a cathode cell. The anode cell, which is a porous pot, contains a 20% solution of sodium carbonate. The cathode and the anode are both of nickel gauze.

The mixture is first warmed to 75°, and the high current keeps it boiling. Alcohol may be added from time to time to replace that evaporated. The current density is 15 amperes, and the E.M.F. 7—8 volts. After about 20 ampere hours have passed, the current density is cut down to 2 amperes. After 24 ampere hours have passed, the current is stopped; the hot cathode liquid is then poured into a mixture of 50 c.cs. of sulphuric acid and 100 c.cs. of water, and allowed to stand. The *p*-phenylenediamine sulphate is filtered and dried on a porous plate.

*Yield.*—75% theoretical (10 gms.). *o*-Nitroaniline gives by same method *o*-phenylenediamine; *m*-nitroaniline gives by same method 3 : 3′-diaminoazobenzene. (B., 28, 2350.)

PREPARATION 412.—**Borneol.**

$$C_{10}H_{18}O. \qquad 154.$$

A 10% solution of camphor in alcohol and half its volume of 75% sulphuric acid is placed in the cathode chamber and 70% sulphuric acid placed in the anode chamber. The current density is 12 amperes, and the E.M.F. 10—15 volts. The current is allowed to pass for 5 hours, the temperature being kept below 20°. The product is then poured into water, and the solid filtered off, dried and recrystallised from petroleum ether.

*Yield.*—40% theoretical. M.P. 204°—205°. (Z.e., 8, 288.)

PREPARATION 413.—**Diethyl Adipate** [*Di-ethyl ester of hexan di-acid*].

$$COOC_2H_5.(CH_2)_4.COOC_2H_5. \qquad C_{10}H_{18}O_4. \qquad 202.$$

**Ethyl Acrylate.**

$$CH_2 : CH.COOC_2H_5. \qquad C_5H_8O_2. \qquad 100.$$

A nearly saturated solution of potassium ethyl succinate (1·5 parts of salt to 1 part of water) is placed in a tall beaker, which must not be more than half full, and which should be cooled in ice-water. An anode of stout platinum wire, made into a spiral, is introduced. The cathode consists of a piece of sheet platinum. A current of 50—75 amperes per sq. dcm. of anode surface is then passed through. Much frothing takes place. At the end of the reaction—70 c.cs. of solution require 20 ampere hours—the mixture with the adipic ester floating on the surface is diluted with water in a separating funnel, and extracted twice with ether. The ethereal extract is dried over calcium chloride and placed in a distilling flask. After removing ether, the fraction distilling up to 120° containing ethyl acetate is separately collected. The residue containing diethyl adipate is distilled under reduced pressure.

$$\begin{matrix} COOC_2H_5.CH_2CH_2\,\vdots\,COO\,\vdots\,K \\ COOC_2H_5.CH_2.CH_2\,\vdots\,COO\,\vdots\,K \end{matrix} \rightarrow \begin{matrix} COOC_2H_5.CH_2.CH_2 \\ \qquad\qquad\qquad | \\ COOC_2H_5.CH_2.CH_2 \end{matrix} + 2CO_2 + 2K^+.$$

*Yield of Diethyl Adipate.*—30—35% theoretical; B.P. $^{760}$ 245°; colourless liquid with characteristic odour. Ethyl acrylate, which is a by-product, is obtained in only very low yield; B.P. $^{760}$ 101°—102°. (T. R. S. E., 36, 211.)

For a theoretical treatment of electrolytic oxidation and reduction, see text-book of this title by Glasstone and Hickling (1935).

## CHAPTER XXIX

### PRODUCTS FROM NATURAL SOURCES

PREPARATION 414.—**Quinine Sulphate.**

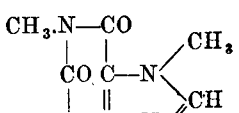
$$C_{20}H_{24}N_2O_2.H_2SO_4 + 8H_2O.$$

80—100 gms. of powdered cinchona bark are placed in a mortar and ground up with about 250 c.cs. of milk of lime. The whole is evaporated to dryness on the water bath, and the mass powdered up when cold. This residue is shaken up with about 200 c.cs. of chloroform, and allowed to stand in a flask for about 12 hours. It is then filtered and washed with chloroform. The quinine is removed from the chloroform extract by shaking up 2 or 3 times with dilute sulphuric acid and then with water, until the aqueous solution no longer exhibits a blue fluorescence. The acid and aqueous extracts are carefully neutralised with ammonia, and the whole is evaporated on the water bath until quinine sulphate begins to separate out; it is filtered off, on cooling. Another crop of crystals may be obtained by concentrating the mother liquor. The quinine sulphate may be recrystallised from water.

*Yield.*—1—2 gms.

The free base may be isolated by dissolving the sulphate in water slightly acidified with dilute sulphuric acid. Excess of sodium carbonate solution is then added, when the quinine is precipitated. It is filtered off, washed and dried. M.P. 175°.

PREPARATION 415.—**Caffeine** (1 : 3 : 7-*Trimethylxanthine*).



$C_8H_{10}O_2N_4$. 194.

$\frac{1}{4}$ lb. of tea is boiled up with 600 c.cs. of water for 15 minutes, and filtered through fine cotton, the leaves being washed with about 300 c.cs. of boiling water.

The filtrate is heated to boiling, and basic lead acetate (made by boiling lead acetate with litharge and water, and filtering) is added until no further precipitation of the albumins and tannins present takes place. This is filtered and the residue washed with hot water. The lead in the filtrate is precipitated by adding dilute sulphuric acid. The clear liquor is decanted from the lead sulphate and concentrated to about 300 c.cs., animal charcoal being added. After filtering and cooling, the filtrate is extracted several times with chloroform. The chloroform is removed by distillation on the water bath, and the crude product boiled up with water

and animal charcoal, and filtered. The filtrate is then concentrated until crystallisation takes place.

*Yield.*—1—2 gms. Fine needles, containing $1H_2O$; M.P. 234°—235°. Caffeine may be synthesised from uric acid. (D.R.P., 121224.)

PREPARATION 416.—*d*-**Alanine** [*d-2-Amino-propan acid*].

$$CH_3.CH(NH_2)COOH. \qquad C_3H_7O_2.N. \qquad 89.$$

**Glycocoll-ester Hydrochloride** [*Hydrochloride of ethyl ester of amino-ethan acid*].

$$CH_2(NH_2.HCl.).COOC_2H_5. \qquad C_4H_{10}O_2.N.Cl. \qquad 139{\cdot}5.$$

The raw material employed is the cheap waste of raw Milan silk, 500 gms. of which are treated with 2 litres of fuming hydrochloric acid (D. 1·19) and frequently shaken until in the course of an hour the threads have fallen to pieces. The flask is warmed, with frequent shaking, on a steam bath; the liquid foams considerably, and a dark violet solution is produced. This is boiled under a reflux condenser for 6 hours; it is advisable to add a few gms. of animal charcoal. When quite cold, the acid liquor is filtered through a coarse but strong filtering cloth, and evaporated under reduced pressure (10—15 mm.) at 40°—45° to a thick syrup. This is treated while still warm with 3 litres of absolute alcohol, and a very rapid current of dry hydrogen chloride passed in without cooling and with frequent shaking, until the liquid is saturated. In this process complete solution should occur, and the alcohol should boil. The operation is usually finished in $1\frac{1}{2}$ hours. If the current of hydrogen chloride, and consequently the rise in temperature, is too small, the mixture must be boiled afterwards for $\frac{1}{2}$ hour on the water bath, in order to render the esterification as complete as possible.

The very dark brown liquid is now cooled to 0°, and "inoculated" with a few small crystals of glycocoll-ester hydrochloride, and the greater part of the glycocoll-ester hydrochloride separates in the course of 12 hours at 0° in the form of a thick paste of crystals. The mass is filtered at the pump through coarse linen, well pressed, and washed with a little ice-cold alcohol. The acid alcoholic solution is evaporated as completely as possible under low pressure from a bath at 40°—45°, and the residual syrup is again esterified with $1\frac{1}{2}$ litres of alcohol and hydrogen chloride, as before. The cold solution is "inoculated," and allowed to stand for 2 days at 0°, when the remainder of the glycocoll is for the most part precipitated as ester hydrochloride. The solution, after filtration, is again evaporated under reduced pressure. The syrup left behind contains the hydrochlorides of the other amino-acid esters. In order to liberate the esters, the residue is dissolved by vigorous shaking at ordinary temperature in the smallest quantity of water (about $\frac{1}{4}$ volume). To the solution is added about twice its volume of ether, and the whole is carefully cooled in a freezing mixture. Strong caustic soda is then cautiously added until the free acid is almost neutralised, and, finally, a saturated solution of potassium carbonate. On vigorous shaking, a considerable part of the liberated esters goes into solution in the ether. The ether is now poured

off and replaced by fresh ether. The whole is carefully cooled, then an excess of concentrated alkali is added, and immediately afterwards potassium carbonate in small portions, until the whole mass has become a thick paste. The ether is repeatedly renewed during the operation. The extraction with ether is continued until the extracts are colourless. This requires 4—5 litres of ether.

The united ethereal solutions, which are brown in colour, are shaken for 5 minutes with potassium carbonate, then poured off, and dried for 12 hours over anhydrous sodium sulphate. When the greater part of the ether has been evaporated at ordinary pressure on a water bath, the distillation is continued under a pressure 10—12 mms. At ordinary temperature, ether first passes over. The distilling vessel is now warmed in warm water, when a first fraction is obtained, which still contains alcohol and ether, and also some glycocoll ester and alanine ester. When the temperature of the bath has risen to 55°, the main part of the alanine ester begins to boil. The operation is discontinued when, at a bath temperature of 80°, nothing more distils over. In this way 110—125 gms. distillate are obtained, consisting for the most part of alanine ester.

To obtain free alanine the alanine ester is heated for about 6 hours with 5 times its weight of water on a water bath, until the alkaline reaction has disappeared. The solution is evaporated on a water bath till crystallisation begins. The liquid is allowed to stand at 0°, when about 30 gms. alanine separate; optical examination shows this to consist of almost pure *d*-compound. From the mother liquor a second crop of 20—25 gms. may be obtained, and this still consists of fairly pure active amino-acid, so that the total yields amount to 50—55 gms. The last mother liquor still contains a fair amount of active alanine, but it is mixed with so much racemic substance that it cannot be separated from it by mere recrystallisation from water. The first two crops are dissolved once more in hot water, and the liquid evaporated on the water bath till it begins to crystallise. At 0° a large quantity of the pure, active amino-acid separates out.

*Glycocoll-ester hydrochloride*: Colourless needles; soluble in hot alcohol; very soluble in water; M.P. 144°. *D-alanine*: Needles; soluble in water; decomposes on heating; $[\alpha]_D^{20}$ (hydrochloride) $= + 9{\cdot}55°$. (J. pr., [2], 37, 160; B., 27, 60; 32, 2459; O. S., IX., 4; C. r., 186, 1844.)

PREPARATION 417.—**Cystine** [*Di-(2-amino-2-carboxy-ethanyl-(1))- disulphide*].

$$\left.\begin{array}{l}HOOC.CH(NH_2).CH_2S\\HOOC.CH(NH_2).CH_2S\end{array}\right\rangle \quad C_6H_{12}O_4N_2S_2. \qquad 240.$$

500 gms. of horsehair are boiled in a flask of 3 litres capacity with $1\frac{1}{2}$ litres of conc. hydrochloric acid (about 30% strength) for 6 hours under a reflux condenser. The dark coloured liquid is diluted with 4 litres of water, and, while kept fairly cool, is treated with conc. potassium hydroxide solution (33%) until the reaction is only faintly acid. To

clarify the liquid it is warmed and vigorously stirred for some time with about 40 gms. of animal charcoal, and filtered. The filtrate is exactly neutralised with potassium hydroxide, and set aside to crystallise at low temperature, preferably in the ice chest, for 5—6 days. The cystine which separates is filtered at the pump, washed with cold water, then dissolved in the smallest possible quantity of warm 10% ammonia, again treated with animal charcoal in the warm, and finally precipitated from the filtrate by the addition of acetic acid. This operation is repeated once more; the final product is quite colourless and free from tyrosine.

*Yield.*—15 gms. Colourless crystals. (E. Fischer, "Organic Preparations," 1908; O. S., V., 39.)

PREPARATION 418.—**Glucosamine Hydrochloride** [*Hydrochloride of* 2-*Amino*-3 : 4 : 5 : 6-*tetrol-hexanal*- (1)].

$CH_2OH.(CHOH)_3CH(NH_2 : HCl).CHO.$ $C_6H_{14}O_5Cl.$ 191·5.

The carapaces and claws of lobsters, which have been cleaned, as far as possible mechanically, are digested for 24 hours with cold dilute hydrochloric acid. They may then be cut up easily, and freed from adherent fibres and flesh. 100 gms. of the material thus prepared are covered in a porcelain dish with fuming hydrochloric acid, and heated to gentle boiling on a sand bath. The chitin quickly goes into solution, and the liquid becomes dark in colour. The liquid is evaporated until a considerable crystallisation of glucosamine hydrochloride has taken place, then allowed to cool, filtered at the pump, through linen or hardened paper, and washed with a little cold hydrochloric acid. The mother liquor, on further evaporation, yields a second crop of crystals. To purify the salt it is dissolved in warm water, and the solution concentrated till crystallisation begins.

Colourless crystals; soluble in hot water. (B., 17, 213.)

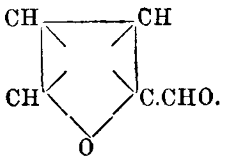
PREPARATION 419.—**Tyrosine** [2-*Amino*-3-(*p-hydroxyphenyl*)-*propan acid*].

$HO.C_6H_4.CH_2.CH(NH_2).COOH.$ $C_9H_{11}O_3.$ 167.

100 gms. of silk waste are boiled for 6 hours under a reflux condenser with 300 c.cs. of fuming hydrochloric acid (D. 1·19). The greater part of the hydrochloric acid is removed by evaporating the brown coloured solution under reduced pressure; the residue is dissolved in water, filtered, and made up to a known volume. The percentage of hydrochloric acid is determined by titration of an aliquot part of the liquid, and the amount of sodium hydroxide calculated for the whole solution is then added, with ice cooling and constant stirring. A brownish-black precipitate is at once produced. After it has stood for an hour in ice-water, it is filtered off at the pump, dissolved again in hot water, and boiled vigorously with about 10 gms. of animal charcoal. The filtered liquid is now colourless, and deposits pure tyrosine on cooling. By concentrating the mother liquor a second crop of crystals may be obtained.

*Yield.*—5—6 gms. Colourless crystals: soluble in hot water. (Z. ph., 48, 528.)

PREPARATION 420.—**Furfuraldehyde** (*Furfurol*).



$C_5H_4O_2$. 96.

A mixture of 200 gms. of bran, 200 gms. of conc. sulphuric acid, and 600 gms. of water is distilled from a large flask till the distillate measures about 600 c.cs. The latter is neutralised with caustic soda, mixed with 150 gms. of common salt and again distilled, till about 200 c.cs. have passed over. The distillate is again saturated with common salt, extracted with ether, the extract dried over anhydrous sodium sulphate, the ether removed on the water bath, and the residue distilled, the fraction 160°—165° being collected separately.

*Yield.*—6 gms. Colourless liquid; characteristic smell; darkens on standing; B.P. 162°. (A., 74, 280; 116, 258; O. S., I., 49.)

PREPARATION 421.—**Oleic Acid** [9-*Octadecen Acid*].

$$CH_3(CH_2)_7CH = CH(CH_2)_7COOH. \qquad C_{18}H_{34}O_2. \qquad 282.$$

10 gms. of potassium hydroxide in 100 c.cs. of alcohol are heated with 30 gms. olive oil for 1—2 hours under a reflux. The alcohol is removed on a water bath, and dilute acetic acid is added to the residue until it is neutral to phenolphthalein. 30 gms. of conc. lead acetate solution are then added; this precipitates a mixture of the lead salts of oleic, palmitic, and stearic acids. The mixture is filtered and washed with alcohol to remove unchanged oil. It is then extracted in a Soxhlet apparatus with ether, which dissolves lead oleate. When the ether is evaporated lead oleate remains. Pure dilute nitric acid is added, and oleic acid separates as an oil. The oil is removed by means of a separating funnel, dried over calcium chloride, and distilled under reduced pressure.

$$C_3H_5(O.COC_{17}H_{33})_3 + 3KOH \rightarrow 3C_{17}H_{33}COOK + C_3H_5(OH)_3.$$

Colourless oil; M.P. 14°; B.P. $^{10}$ 223°; decomposes on heating at ordinary pressure; D. $^{15}_{4}$ 0·895. (B., 27, 172.)

# CHAPTER XXX

## STEREOCHEMICAL REACTIONS

PREPARATION 422.—**α-Bromocinnamic Acid** [3-*Phenyl-2-bromo-2-propen acid*].

$$C_6H_5.CH : CBr.COOH. \qquad C_9H_7O_2Br. \qquad 227.$$

5 gms. of pure α-bromo-*allo*cinnamic acid (p. 419) are placed in a test tube with a thermometer immersed in the substance. The tube is immersed in a bath of conc. sulphuric acid heated to 200°—210°, and kept there for 10 minutes. After cooling, the product is dissolved in dilute alkali, and after neutralising the excess of alkali the solution is treated with a solution of barium chloride, which precipitates the barium salt of α-bromocinnamic acid. The free acid can be liberated in the usual way.

$$\begin{array}{ccc} C_6H_5CH & & C_6H_5CH \\ \| & \rightleftarrows & \| \\ Br.C.COOH & & COOH.C.Br \\ \text{α-Bromocinnamic acid.} & & \text{α-Bromo-}\textit{allo}\text{cinnamic acid.} \\ \text{M.P. 131°.} & & \text{M.P. 120°.} \end{array}$$

*Yield.*—80—85% theoretical (4—4·2 gms.). Colourless prismatic needles; soluble in hot benzene; M.P. 131°. (J. C. S., 83, 686.)

PREPARATION 423.—**Mesaconic Acid** [trans-3-*Carboxy-2-buten acid*].

$$\begin{array}{l} \quad CH_3 \\ \quad | \\ \quad C.COOH. \qquad C_5H_6O_4. \qquad 130. \\ \quad \| \\ HOOC.C.H \end{array}$$

20 gms. of citraconic acid (see p. 243) are dissolved in the minimum quantity (about 25 c.cs.) of pure dry ether in a quartz flask. 5 gms. of chloroform and a few drops of a moderately strong solution of bromine in chloroform are then added. The solution is exposed to strong sunlight, or to the rays of a mercury vapour lamp. Mesaconic acid soon begins to separate on the side of the flask nearest the light. The flask is occasionally turned, and drops of bromine are added at intervals until no further separation takes place. The pasty mass is filtered, washed with ether and dried.

$$\begin{array}{ccc} CH_3 & & CH_3 \\ | & & | \\ C.COOH & \rightarrow & C.COOH \\ \| & & \| \\ CH.COOH & & HOOC.C.H \end{array}$$

*Yield.*—73% of complete conversion (15 gms.). Colourless crystals; M.P. 202°; somewhat soluble in water; insoluble in ether and in chloroform. (A., 188, 73.) See also O. S., XI., 74.

PREPARATION 424.—**Benz*anti*aldoxime** (*β-Benzaldoxime*).

$$\begin{array}{c} C_6H_5CH \\ \| \\ HO.N \end{array} \quad C_7H_7ON. \quad 121.$$

12 gms. α-benzaldoxime (p. 288) are dissolved in 50 c.cs. pure anhydrous ether. Dry hydrogen chloride is passed into this solution, using a rather wide delivery tube, since the hydrochloride of the β-oxime, which separates quickly, is liable to block the end of the tube. The precipitate is filtered off, washed with ether, transferred to a separating funnel and mixed with 50 c.cs. of ether. Conc. sodium carbonate solution is then added, with shaking, until effervescence ceases. The ethereal layer, which contains the β-oxime, is separated from the lower aqueous sodium chloride layer, dried over anhydrous sodium sulphate, and the ether removed in a vacuum desiccator. The residue forms a mass of small needles, which are pressed out on a porous plate.

*Yield.*—80% theoretical (8 gms.). M.P. 128°—130° (on quick heating). (B., 23, 1684.)

$$\begin{array}{c} C_6H_5CH \\ \| \\ NOH \end{array} \longrightarrow \begin{array}{c} C_6H_5.CH \\ \| \\ HO.N \end{array}$$

PREPARATION 425.—**Resolution of Mandelic Acid.**

$$\begin{array}{c} COOH \\ | \\ H—C—OH. \\ | \\ C_6H_5 \end{array} \quad C_8H_8O_3. \quad 152.$$

25 gms. *r*-mandelic acid in 30 c.cs. absolute alcohol are added slowly to a warm solution of 25 gms. ephedrine (lævo) in 45 c.cs. absolute alcohol. The whole is gently warmed (not boiled) for 2 hours on a water bath and cooled in the ice-chest overnight. The crystals of (—) ephedrine (—) mandelate are filtered, washed with 15 c.cs. absolute alcohol and then boiled with 30 c.cs. absolute alcohol. On cooling, the complex is filtered, drained, and mixed with excess hydrochloric acid until definitely acid to Congo red. The (—) mandelic acid is extracted with ether (six times), the aqueous layer being finally acid to Congo red. The ether extract (dried over anhydrous sodium sulphate) yields about 11 gms. (—) mandelic acid, $[\alpha]_{5461} = -177°$ in acetone. The aqueous layer is made alkaline with *excess* of strong caustic soda solution and the (—) ephedrine extracted (4 times) with ether. The ethereal solution is dried over anhydrous sodium sulphate and the (—) ephedrine recovered by distillation of the ether.

The alcoholic filtrate and washings from the above resolution can be united, split into two parts, and 20 gms. *r*-mandelic acid dissolved in one and 20 gms. of (—) ephedrine in the other. The two solutions are slowly mixed, warmed on a water bath for an hour, cooled, when (—) ephedrine (—) mandelate appears. This is treated as above and 10 gms. (—) mandelic should be obtained ($[\alpha]_{5461} = -147°$ in acetone). With the

filtrate and washings from this second crop another resolution with 20 gms. *r*-mandelic acid and 20 gms. (—) ephedrine can be effected. This gives a third crop (12 gms.) of (—) acid ($[\alpha]_{5461} = -78{\cdot}3°$ in acetone).

Finally, the alcohol is removed from the filtrate and washings under diminished pressure on the water bath. The syrupy residue is dissolved in hydrochloric acid and (+) acid extracted with ether when 22 gms. (+) acid, $[\alpha]_{5461} = +160°$ in acetone, are obtained.

The first crop of (—) mandelic acid is recrystallised from benzene containing acetone, when it yields 7·5 gms. pure (—) mandelic acid, $[\alpha]_{5461} = -190°$. The second and third crops of (—) acid can be recombined with (—) ephedrine as described above, yielding a further 15 gms. of pure (—) mandelic acid. The crude (+) acid after recrystallisation from benzene-acetone gives 15 gms. (+) acid, $[\alpha]_{5461} = +190°$ in acetone. (J., 1935, 1544.) Colourless needles, M.P. 133°—134°.

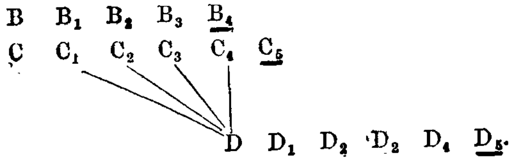
*r*-mandelic gives (+) acid by resolution with cinchonine (B., 16, 1773; 32, 2385), and the (—) acid by resolution with morphine. (J., 1899, 75, 753.)

PREPARATION 426.—**Resolution of α-Phenylethylamine.**

$$\begin{matrix} C_6H_5 \\ CH_3 \end{matrix}\!\!>\!CH.NH_2. \qquad C_8H_{11}N. \qquad 121.$$

*Dextro-base.*—165 gms. of dry *lævo*-malic acid are covered with 660 c.cs. of cold water in a beaker. 148 gms. of racemic α-phenylethylamine (p. 366)—necessary to form the acid salt—are then added, during a few minutes with constant stirring. Both base and acid dissolve, but before the acid has completely disappeared the solution becomes slightly syrupy, and a crystalline powder begins to separate. The mass is stirred with a glass rod until the malic acid is all dissolved, and then left to stand overnight. The crude *l*-malate of *d*-α-phenylethylamine is filtered off with suction, well pressed down, and washed with a little cold water. [The mother liquor A, containing chiefly the *l*-malate of *l*-α-phenylethylamine, is reserved for the preparation of the *l*-amine (see below).] The crude salt, which, when dry, is approximately equal in weight to that of the phenylethylamine used, is recrystallised 3 or 4 times from water. The following method is convenient (p. 13): the crude salt is divided into two portions, B and C. B is dissolved in the minimum of hot water (not above 90°), filtered hot, if necessary, and set aside to crystallise; the formation of small crystals should be induced by cooling in ice-water and scratching with a glass rod. When no more crystals separate, the crop $B_1$ is filtered off, and the filtrate and small quantity of washings used to recrystallise C, from which crop $C_1$ is obtained. $B_1$ is recrystallised in the minimum of hot water, yielding crop $B_2$, and a mother liquor, which is used to recrystallise $C_1$. The recrystallisation is continued in this manner until crops $B_4$ and $C_4$ are obtained. $B_4$ is pure *d*-amine-*l*-malate, M.P. 184°. The mother liquors from $C_1$, $C_2$, $C_3$ and $C_4$ are combined and evaporated to about $\frac{1}{4}$ of their volume, then cooled in ice-water, and

the resulting crop of crystals D filtered off. $C_4$ is recrystallised once more from fresh hot water, and the mother liquor from $C_5$ is used to recrystallise D. $C_5$ is pure, and $D_1$ is recrystallised 4 more times from water, after which it is pure.




If large quantities of salt are being recrystallised, the mother liquors of $D_1$—$D_5$ should be worked up after the above manner to yield more *d*-amine-*l*-malate. The yield of pure *d*-amine-*l*-malate should be about 70% (76·5 gms.) of the crude product. The pure salt is dissolved in water, the solution placed in a separating funnel, and caustic soda solution (30%) added so long as any turbidity of the aqueous layer is produced. The upper layer of base is separated, and the lower aqueous layer extracted with ether to recover any dissolved base. The ethereal extract is united with the base and dried over anhydrous sodium sulphate. The ethereal solution is introduced, in portions at a time, to a Claisen distilling flask of appropriate size, and the ether distilled off (see p. 36). The residue is then distilled in an apparatus filled with hydrogen, the fraction 180°—190° being collected. For polarimetric observations the amine should be distilled directly into a polarimeter tube, as it is a strong base which absorbs carbon dioxide with avidity.

*Yield.*—90% theoretical (calculated on pure malate), or 30% of the weight of racemic base used. B.P. 186°—187°; $[\alpha]_D^{17^\circ} = + 41{\cdot}59^\circ$; $D.^{17}$ 0·9502.

In the above resolution an equivalent amount of the carbamate of the base can be used in place of the free base.

*Lævo-base.*—The solution A (referred to above) plus the mother liquors from the recrystallisation of the malate is treated with an excess of caustic soda (50%) to liberate the base, which is extracted with ether, the dark brown colour of the liberated amine being discharged by standing in contact with potash and ether. The base obtained gives $\alpha = 20^\circ$ in a 1 dcm. tube at 15°, which corresponds with an *l*-base content of about 75%. To purify it further, it (60 gms.) is slowly poured, with stirring, into a solution of tartaric acid (75 gms.) in warm 96% alcohol (1,000 c.cs.). After standing overnight the mixture solidifies completely, but the mass is not crystalline, having rather the nature of a gel. It is heated gently on a water bath to 60°, when it becomes liquid, containing a deposit of heavy, colourless, prismatic crystals, which are collected and washed with alcohol at 50°—60°. The mother liquors on cooling set to a firm, gel-like mass, which can easily be liquefied by heating to 40°.

The prisms are dissolved in fresh 96% alcohol by heating under reflux for a considerable time, as they are not very soluble, even at the boil.

After cooling, the crystals are collected and washed with warm alcohol. 78 gms. (47% theoretical) of *l*-amine-*d*-tartrate are thus obtained. This salt forms colourless, monoclinic prisms, very soluble in water (from which it may readily be recrystallised); sparingly soluble in 96% alcohol; almost insoluble in absolute alcohol. M.P. 192°—193·5° (sharp).

The *l*-base liberated (compare *d*-base for fuller details) from this salt by 30% potash, after drying and distillation in a current of hydrogen, gave $[\alpha]_D^{15°} = -41·48°$. (J. R. T. C., 1926, 65.)

## Note

At the present time commercial malic acid is chiefly produced by the hydration of maleic anhydride obtained by oxidation of benzene (p. 247) and is optically inactive. Accordingly, a method has been devised whereby the amine can be resolved by the use of tartaric acid (G., 1920, 50, 276; Archiv der Pharmazie and Berichte der Deutschen Pharmazeutischen Gesellschaft, 1935, 408).

The amine (121 gms.) is added slowly to a solution of tartaric acid (150 gms.) in 750 c.cs. methyl alcohol. After cooling, the complex is immediately filtered and recrystallised from boiling methyl alcohol (2 litres). The complex is decomposed in the usual manner, when pure amine, $\alpha_{5893}^{20} = -38·7°$, is obtained.

The methyl alcohol is removed from the filtrate and the residue recrystallised from water. In this crystallisation it may be necessary to concentrate and cool the solution in ice. Two or three re-crystallisations from water may be necessary. The complex obtained yields amine of $\alpha_{5893}^{20} = +37°—38°$.

# CHAPTER XXXI

## DECOMPOSITIONS

Preparation 427.—**Butyric Acid** [*Butan Acid*].

$CH_3.CH_2.CH_2.COOH.$ $C_4H_8O_2.$ 88.

10 gms. of ethylmalonic acid (p. 241) are introduced into a small distilling flask, which is placed in an oil bath with the side tube sloping upwards. A cork, carrying a thermometer with bulb immersed in the substance, is inserted in the neck of the flask. The substance is heated at 180° until no further carbon dioxide is evolved. The side tube of the flask is then sloped downwards and the product (butyric acid) distilled, the fraction 160°—165° being collected.

$$CH_3.CH_2CH(COOH)_2 \rightarrow CH_3.CH_2.CH_2.COOH + CO_2.$$

*Yield.*—85% theoretical (5·5 gms.). Colourless liquid; rancid odour; B.P. 162·3°; D. $^{161\cdot5}_{4}$ 0·8141. (A., 138, 218; J., 1868, 514.)

Preparation 428.—**Pyrogallol** (1 : 2 : 3-*Trihydroxybenzene*).

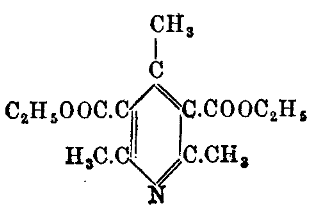
$C_6H_3(OH)_3.$ $C_6H_6O_3.$ 126.

10 gms. of gallic acid and 20 gms. of powdered pumice are mixed and placed in a retort. A cork, carrying a delivery tube, is inserted through the tubulus to serve for the entrance of carbon dioxide. The retort is then heated on a sand bath with a stream of carbon dioxide passing through, the stem of the retort sloping downwards into a receiver. Crystals of pyrogallol condense in the stem, which should be warmed with a small flame to cause the product to melt and flow down into the receiver.

$$C_6H_2(OH)_3.COOH \rightarrow C_6H_3(OH)_3 + CO_2.$$

*Yield.*—40% theoretical (3 gms.). Colourless crystals; M.P. 133°; soluble in alcohol, ether and water. (A., 101, 48.)

Preparation 429.—**Diethylcollidine dicarboxylate** (2 : 4 : 6-*Trimethyl-3 : 5-dicarbethoxy-pyridine*).




$C_{14}H_{19}O_4N.$ 265.

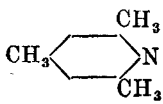
20 gms. of ethyldihydrocollidinedicarboxylate (see Preparation 93) and 20 gms. alcohol are placed in a small flask, which is immersed in a bath of cold water. Nitrous fumes (p. 507) are led into the mixture until a test

sample dissolves to a clear solution in dilute hydrochloric acid. The alcohol is then evaporated off on a water bath, the residue treated with sodium carbonate until alkaline, and the oil which separates extracted with ether. The ethereal extract is dried over potassium carbonate, the ether evaporated, and the residue distilled. The fraction 290°—310° is collected and redistilled, the pure ester distilling at 308°—310°.

$$C_5H_2N(CH_3)_3(COOC_2H_5)_2 + O \rightarrow C_5N(CH_3)_2(COOC_2H_5)_2 + H_2O.$$

*Yield.*—80% theoretical (16 gms.). Yellow oil; B.P. 308°—310°. (A., 215, 8.)

PREPARATION 430.—**Collidine** (2 : 4 : 6-*Trimethylpyridine*).



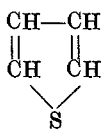
$C_8H_{11}N$. 121.

10 gms. of powdered dry dipotassium collidine dicarboxylate (see Preparation 181) are intimately mixed with 20 gms. of slaked lime, and the mixture introduced into a 50-cm. length of combustion tubing, closed at one end. A loose plug of asbestos is placed in the open end of the tube, the tube is tapped horizontally on the bench to make a passage for gas and then connected by means of an adapter to a small receiver. The tube is placed in a sloping combustion furnace, so that the sealed end is slightly elevated. The closed end is first heated, the rest gradually, and finally the whole length is strongly heated with the tiles in position. The distillate is taken up with ether, the extract dried over solid potassium hydroxide and distilled, the fraction 169°—174° being separately collected.

$$C_5N(CH_3)_3(COOK)_2 + 2Ca(OH)_2 \rightarrow 2CaCO_3 + 2KOH + C_5NH_2(CH_3)_3.$$

*Yield.*—Almost theoretical (4 gms.). B.P. 172°; greenish-yellow liquid with an obnoxious odour. (A., 215, 32.)

PREPARATION 431.—**Thiophen** [1 : 3-*Di-en*-1 : 4-*butylene sulphide*].



$C_4H_4S$. 84.

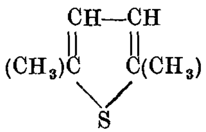
100 gms. (less than 1 mol.) of phosphorus trisulphide (p. 505) and 100 gms. (1 mol.) of thoroughly dry sodium succinate are intimately mixed and placed in a 500-c.c. retort, to which is attached a tube for passage of carbon dioxide throughout the operation. The retort is connected to a condenser, which passes through a cork to a receiver cooled in a freezing mixture. A wash-bottle containing dilute caustic soda and fitted with a cork carrying two delivery tubes is connected on one side to the receiver, and on the other to a draught chamber (or a slight suction from a pump). On heating the retort with a small flame a reaction soon commences, and the mass swells up with the evolution of much sulphuretted hydrogen. At this stage the flame is withdrawn and the reaction allowed to proceed spontaneously until completion (*e.g.*, till gas

ceases to bubble through the wash-bottle). The contents of the receiver are distilled from a water bath, washed with dilute caustic soda, dried over metallic sodium and redistilled.

$$(CH_2.COONa)_2 + 4H_2S \rightarrow C_4H_4S + Na_2S + 2S + 4H_2O.$$

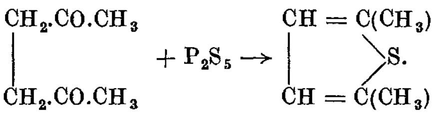
*Yield.*—30% theoretical (15 gms.). Colourless liquid; faint smell resembling that of benzene; B.P. 84°. Gives blue colour (indophenine) with isatin and conc. sulphuric acid. (B., 18, 454; O. S., XII., 72.)

PREPARATION 432.—**Thioxene** (1 : 4-*Dimethylthiophen*).



$C_6H_8S$. 112.

6 gms. (1 mol.) of acetonyl-acetone (see p. 194) are heated with 4 gms. (excess) of finely powdered phosphorus pentasulphide in a sealed tube at 140°—150° for an hour. On cooling, a colourless liquid and a solid are obtained; the former is poured off and fractionally distilled. The distillation is repeated over metallic sodium, the fraction 132°—136° being retained.



*Yield.*—50% theoretical (3 gms.). Colourless, mobile liquid; characteristic odour; B.P. 135°; D. $^{17.5}_{4}$ 0·9755; gives a cherry-red colour with a solution of isatin in conc. sulphuric acid. (B., 18, 2251; 20, 1747.)

PREPARATION 433.—**Phenyl*iso*thiocyanate** (*Phenyl mustard oil*).

$C_6H_5NCS$. $C_7H_5NS$. 135.

64 c.cs. conc. hydrochloric acid and 20 gms. thiocarbanilide are boiled for 30 minutes in a flask attached to a reflux condenser, when the phenyl isothiocyanate separates as an oil. 40 c.cs. water are added and the whole distilled until about 15 c.cs. remain in the flask. The distillate is extracted with ether, which is then dried with calcium chloride. The ether is removed by distillation, and the fraction boiling at 197°—222° collected. This is redistilled, and the fraction 218°—222° retained.

$$(C_6H_5NH)_2CS \xrightarrow{HCl} C_6H_5NCS + C_6H_5NH_2(HCl).$$

*Yield.*—55% theoretical (7 gms.). Colourless liquid with pungent odour; B.P. 222°; $D^{15.5}$ 1·135. (Z. Ch., 1869, 589; O. S., VI., 72.)

PREPARATION 434.—**Trimethylethylene** [2-*Methyl-2-buten*].

$(CH_3)_2C : CH.CH_3$. $C_5H_{10}$. 70.

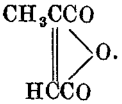
20 gms. of amyl alcohol (from fusel oil) are mixed with 30 gms. of anhydrous zinc chloride in the form of small lumps, left for 24 hours, then heated on a sand bath, the low-boiling distillate being collected and carefully fractionated. The product is a mixture of several isomeric amylenes,

but consists mainly of trimethylethylene. The receiver must be cooled in ice.

$$C_5H_{11}OH—H_2O \rightarrow C_5H_{10}.$$

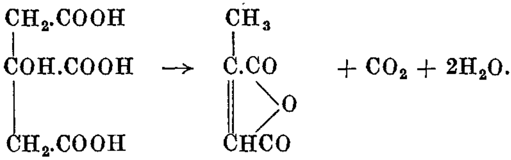
Volatile liquid; B.P. 37°. (A., 128, 225.)

PREPARATION 435.—**Citraconic Anhydride** [*Anhydride of* cis *3-carboxy-2-buten acid*].



$C_5H_4O_3$. 112.

250 gms. of crystallised citric acid are dehydrated by heating in a porcelain basin to a temperature not exceeding 150°. When the acid has become fluid the whole is allowed to cool, removed from the basin and coarsely powdered. The anhydrous acid is then placed in a retort and rapidly distilled. The distillate separates into two layers, the upper layer consisting of water and citraconic acid and the lower layer of impure citraconic anhydride. The layers are separated and the upper layer fractionated, the fraction 190°—210° being collected and added to the anhydride layer. This mixture is distilled under 30 mms. pressure, the fraction 110°—114° being retained.



*Yield.*—22—25% theoretical (30—35 gms.). Colourless liquid; B.P.$^{30}$ 110°—114°; B.P.$^{760}$ 213°—214°. (A., 188, 73.) See also O. S., XI., 28.

PREPARATION 436.—**Ethylene** [*Ethen*].

$$CH_2 : CH_2. \qquad C_2H_4. \qquad 28.$$

50 c.cs. of syrupy *ortho*-phosphoric acid (D. 1·75) are heated until a thermometer in the liquid indicates 210°, and alcohol run in very slowly by means of a dropping funnel drawn out to a point and reaching to the bottom of the flask. During the addition the temperature must be kept between 200° and 220°. The gas is dried by bubbling through conc. sulphuric acid.

$$C_2H_5OH — H_2O = C_2H_4.$$

Colourless gas with sweet smell; sparingly soluble in water, more readily in alcohol and ether; liquefies at 10° and 60 atms. (P. C. S., 17, 147.) See also Preparations 9 and 332.

PREPARATION 437.—**Acetonitrile** (*Methyl cyanide*).

$$CH_3CN. \qquad C_2H_3N. \qquad 41.$$

15 gms. of phosphorus pentoxide are introduced into a 200-c.c. distilling flask attached to a short condenser. As the pentoxide absorbs moisture rapidly and becomes sticky, it is convenient to push the neck of the distilling flask through a cork, which fits the phosphorus pentoxide

bottle, and then to shake the oxide until the required weight is introduced. 10 gms. of powdered acetamide are immediately introduced, the mixture shaken up, and distilled over a small flame, which is constantly moved about. To the distillate is added about half its volume of water, and then solid potassium carbonate, until no more dissolves. The upper layer of liquid, which consists of methyl cyanide, is separated and distilled over a little fresh phosphorus pentoxide.

$$CH_3.CO.NH_2 - H_2O = CH_3CN.$$

*Yield.*—70% theoretical (5 gms.). Colourless liquid; characteristic odour; B.P. 82°. (A., 64, 333; 65, 297.)

PREPARATION 438.—**Acrolein** [*Propenal*].

$$CH_2 : CH.CHO. \qquad C_3H_4O. \qquad 56.$$

200 gms. of glycerine previously dehydrated by heating in an open basin to 170° are mixed with 400 gms. of potassium bisulphate broken to the size of small shot in a glass flask, or better, a metallic retort of at least 4 litres capacity. The delivery tube of the retort is connected to a long condenser to the lower end of which a distillation flask is fastened on tightly (*e.g.*, by means of an adapter).

This latter is surrounded by a freezing mixture, and its side tube connected to a draught pipe. The whole apparatus is fitted up in a fume cupboard.

The mixture is allowed to stand in the closed retort for several days, and then slowly heated and distilled, a gas-ring being used to heat the retort. Water first distils, then the contents of the retort swell considerably, and acrolein mixed with water and sulphurous acid passes over. The distillation is continued till, after several hours, practically no more liquid distils.

The distillate consists of two layers, the upper one being acrolein, the lower an aqueous solution of sulphur dioxide. The latter is removed by shaking with powdered litharge till no more white lead sulphite is formed. The whole mass is again distilled on a water bath, the receiver being cooled, as before, and the same precautions taken to prevent the escape of uncondensed vapours.

The distillate is dried over calcium chloride and again distilled on a water bath. All these operations *must* be carried out in a good fume cupboard, and, to prevent loss by polymerisation, as quickly as possible.

$$CH_2OH.CHOH.CH_2OH \rightarrow CH_2 = CH.CHO + 2H_2O.$$

*Yield.*—30% theoretical (35 gms.). Colourless mobile liquid; penetrating odour; attacks the eyes; polymerises on keeping to a white translucent solid (*disacryl*) resembling porcelain; a small quantity of alkali or a solution of potassium cyanide brings about the change in a few minutes; B.P. 52°. (Bl., 36, 550; A. Ch., [6], 26, 367; O. S., VIII., 120.)

PREPARATION 439.—**Pyruvic Acid** [*Propanon Acid*].

$$CH_3.CO.CO.OH. \qquad C_3H_4O_3. \qquad 88.$$

200 gms. of potassium hydrogen sulphate and 100 gms. of tartaric acid are finely powdered and *intimately* mixed. The mixture is distilled in a short-necked, 2-litre, round-bottomed flask, attached to a moderately long condenser, from a paraffin bath heated to 220°. The apparatus is fitted up in a fume cupboard. The mass froths a great deal at first, and it is necessary to interrupt the heating when the flask is half full of froth, as otherwise it may boil over. When the temperature of the bath has fallen to about 120° the heating is recommenced. The distillation is continued until no more liquid distils. The distillate is at once fractionated under reduced pressure, the fraction 68°—70° at 20 mms. being separately collected. It may also be fractionated at ordinary pressures, the fraction 130°—180° being redistilled and collected at 165°—170°, but it is difficult to obtain it colourless in this way.

$$COOH.CH(OH).CH(OH).COOH = CH_3.CO.COOH + H_2O + CO_2.$$

*Yield.*—50% theoretical (30 gms.). Colourless liquid; polymerises on keeping; has a characteristic odour somewhat resembling that of acetic acid; M.P. 10°; B.P. $^{20}$ 68°—70°; B.P. $^{760}$ 165°; (A., 242, 268; O. S., IV., 63.)

PREPARATION 440.—**Acetaldehyde Ammonia.**

$CH_3CH(OH)NH_2$. $C_2H_7ON$. 61.

The apparatus is set up as shown in sketch (Fig. 56). To the 1½-litre round-bottomed flask is attached a slanting condenser with a long

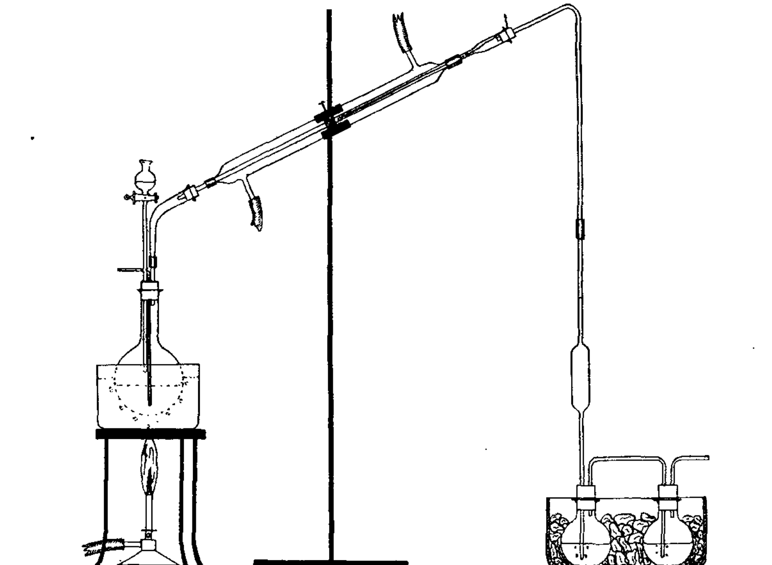


FIG. 56.

delivery tube dipping into 30 c.cs. dry ether in a flask surrounded by a freezing mixture of ice and conc. hydrochloric acid, a further delivery

tube passing into a second flask containing dry ether. A tap funnel is also attached to the flask. A side tube leading below the surface of the liquid in the flask is used for the passage of a moderately strong current of carbon dioxide. A thermometer is suspended in the condenser by a string attached to the cork, with its bulb at the middle. The temperature should be 25°—30°, during the reaction. 100 gms. of ethyl alcohol, 50 c.cs. conc. sulphuric acid, and 80 c.cs. water are placed in the flask and the mixture brought to the boil. A solution of 200 gms. sodium dichromate in 100 c.cs. conc. sulphuric acid and 270 c.cs. water is placed in the dropping funnel while still warm, and dropped at a moderate speed into the alcohol mixture so that boiling is maintained. The funnel should be emptied in about 30 minutes and a further 10 minutes is sufficient to remove the aldehyde. The aldehyde passes over into the ether. Anhydrous sodium sulphate is added to the ethereal solution, which is still kept in the freezing mixture. After a time the solution is decanted and the residue washed with a little dry ether. The solutions are combined, replaced in the freezing mixture, and dry ammonia gas (for preparation, see p. 506) passed through until the solution is saturated. After standing for an hour, the solution deposits crystals, which are filtered off and washed with a little dry ether.

$$3C_2H_5OH + K_2Cr_2O_7 + 4H_2SO_4 \rightarrow 3CH_3.CHO + K_2SO_4 + Cr_2(SO_4)_3 + 7H_2O.$$

$$CH_3CHO + NH_3 \rightarrow CH_3CH(OH)NH_2.$$

*Yield.*—50% theoretical (19 gms.). The compound actually isolated is the trimeride, $(CH_3CHOHNH_2)_3$. (A., 14, 133; J. pr., [1], 76, 54.)

For modifications of the above method, see Am. Soc., 44, 2658; Z. a., 36, 546.

## Dehydrogenation of Primary Alcohols to Yield Aldehydes

When ethyl alcohol is passed over reduced copper at 300°—400°, decomposition takes place into acetaldehyde and hydrogen, the reaction being reversible.

$$CH_3.CH_2OH \rightleftarrows CH_3.CHO + H_2.$$

Methyl alcohol as well as the higher aliphatic and the aromatic alcohols behave similarly. The copper acts catalytically, and while cobalt, nickel, iron, zinc, platinum also serve, copper is the most suitable.

At high temperatures two side reactions accompany the main reaction.

1. The aldehyde formed is split up into hydrocarbon and carbon monoxide.

$$R.CHO \rightarrow RH + CO.$$

2. Dehydration of the alcohol takes place.

$$R.CH_2.CH_2OH \rightarrow RCH : CH_2 + H_2O.$$

The operation should, therefore, be conducted at less than 20° above the lowest temperature at which dehydrogenation proceeds.

Dehydration can be effected catalytically. (E.P., 425,550.)

PREPARATION 441.—**Acetaldehyde.**

$CH_3CHO$. $C_2H_4O$. 44.

A combustion tube 1 metre long is loosely packed for three-quarters of its length with copper oxide (either small lumps or wire form), the layer being held in position with loose asbestos plugs. The tube is placed in a long cylindrical air bath (Fig. 44) fitted with 2 thermometers, preferably nitrogen filled. The oxide is reduced to metal by heating to 180°—200° in a current of specially purified hydrogen. The reduction occupies about 6 days. The hydrogen (from a Kipp) should be passed first through caustic soda solution, then through conc. sulphuric acid, then over heated copper gauze or turnings (previously washed with alcohol to remove grease) to remove arsenic, and finally through a tower containing sticks of caustic soda. On no account must any part of the apparatus be heated until all air has been expelled from the apparatus.

When the reduction is finished, the side tube of a silica distilling flask is connected to the combustion tube, while a dropping funnel is inserted through a cork in the neck of the flask. The other end of the combustion tube is connected first to an empty flask, and then to a worm condenser, which in turn is connected to two suction flasks, cooled in ice and salt. The silica flask is heated in an air bath to 300° while alcohol is dropped in at moderate rate from the tap funnel. At the same time the combustion tube is heated to 300° or even as high as 340°. The vapours from the tube, after condensation, yield unchanged alcohol, a little water, and up to 40% of acetaldehyde ; the escaping hydrogen is led to a draught pipe. After a time, when the catalyst begins to lose its activity, the temperature of the air bath is raised to near 400°.

The aldehyde is separated from the condensed liquid by fractional distillation ; with an efficient column two distillations should give a pure product. The recovered alcohol, after treatment with alkali (to remove traces of acid which always develop) and redistillation, can be again passed over the catalyst.

The highest conversion obtainable with one passage over the catalyst is about 40%, since an equilibrium results at this stage.

The copper loses its activity after some time, but is easily regenerated by oxidation in a current of air at 300°, and subsequent reduction with hydrogen.

$$CH_3CH_2OH \rightleftarrows CH_3CHO + H_2.$$

For use of Cu-carbon catalyst, see C. r., 193, 1189.

PREPARATION 442.—**Benzil.**

$C_6H_5.COCO.C_6H_5$. $C_{14}H_{10}O_2$. 210.

20 gms. of benzoin and 50 c.cs. of conc. nitric acid (D. = 1·42) are placed in a large flask, which is then heated on an actively boiling water bath. A vigorous reaction soon commences, and torrents of nitrous fumes are evolved at first ; for this reason the operation should be conducted in a fume cupboard. After 2 hours' heating, the product is poured into vigorously stirred cold water, the crystalline deposit filtered

off, washed with cold water, pressed out on filter paper and recrystallised from alcohol.

$$C_6H_5.CO.CH(OH).C_6H_5 + O \rightarrow C_6H_5CO.CO.C_6H_5 + H_2O.$$

*Yield.*—80% theoretical (16 gms.). Yellow prisms ; insoluble in water ; M.P. 95°. (A., 34, 188 ; Am. Soc., 51, 2822 ; O. S., I., 25 ; VI., 6.)

PREPARATION 443.—**α-Bromocinnamic** (*cis*) **and α-Bromo*allo*cinnamic** (*trans*) **Acids.**

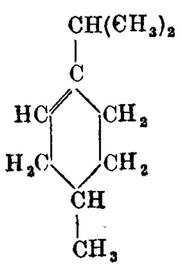
$$C_6H_5CH : CBrCOOH. \qquad C_9H_7O_2Br. \qquad 227.$$

20 gms. (1 mol.) of cinnamic acid dibromide (p. 340) are covered with alcohol and the theoretical amount (2 mols.) of alcoholic potash (say, 70 gms. of a 10% solution) added. After heating for about 15 minutes in a small flask, the mixture is evaporated to dryness in a dish on a water bath. The residue is digested with an amount of water sufficient to dissolve about 75% of the potassium salts, and an excess of a 10% solution of barium chloride added. Barium α-bromocinnamate is precipitated, while barium α-bromo*allo*cinnamate remains in solution. The former is filtered off, washed with dilute barium chloride solution, and the free acid precipitated by treatment with hydrochloric acid ; it is filtered off, washed with water and dried on a porous plate. It is recrystallised from benzene as colourless prismatic needles ; M.P. 131° ; yield 11 gms. The bromo*allo*-acid is recovered in a similar manner by acidifying the solution containing its barium salt. It is recrystallised from petroleum ether as prisms with a yellow tinge ; M.P. 120°.

$$C_6H_5CHBr.CHBr.COOH + 2KOH \rightarrow C_6H_5CH : CBr.COOK + KBr + 2H_2O.$$

(J. C. S., 83, 673.)

PREPARATION 444.—**$\Delta^3$-Menthene.**



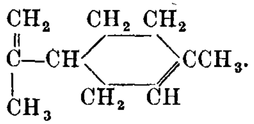
$C_{10}H_{18}$. 138.

70 gms. (1 mol.) of crude menthyl chloride (p. 334) are added to a warm solution containing 75 gms. (excess) of caustic potash dissolved in 320 gms. of phenol. The mixture (contained in a flask) is maintained at 150° for 10—12 minutes, and then distilled until the thermometer (still immersed in liquid) registers 200°. The distillate is placed in a funnel and shaken with dilute caustic soda until free from phenol ; it is then distilled over sodium, the fraction 160°—170° being retained and again distilled over sodium.

$$C_{10}H_{19}Cl + C_6H_5OK \rightarrow C_{10}H_{18} + C_6H_5OH + KCl.$$

Colourless liquid ; B.P. 167° ; D. $^{20}_{4}$ 0·8064. (B., 29, 1843.)

PREPARATION 445.—**Dipentene** ($\Delta^{1\cdot 8}$-*Menthadiene*).



$C_{10}H_{16}$. 136.

10 gms. (1 mol.) of pure dipentene hydrochloride (see p. 341) are carefully heated with 20 gms. (excess) of aniline until the reaction commences, and heating is continued for 2—3 minutes. To the mixture are added 20 c.cs. (excess) of glacial acetic acid, and the excess of aniline removed by steam distillation. Oxalic acid is added to the distillate and steam distillation again effected. The aqueous distillate is separated, the hydrocarbon being dried over solid caustic potash. It is then twice distilled over metallic sodium.

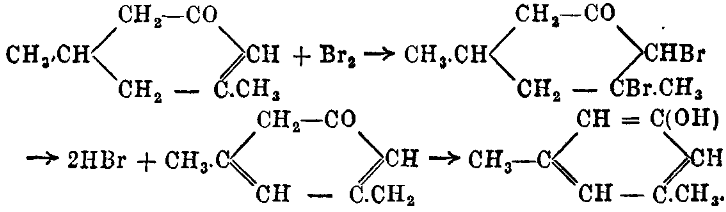
$$C_{10}H_{18}Cl_2 \xrightarrow{-2HCl} C_{10}H_{16}.$$

Colourless liquid; B.P. 178°—180°. (B., 40, 603; A., 245, 196; 350, 150.)

PREPARATION 446.—*s*-**Xylenol** (3 : 5-*Dimethyl*-1-*hydroxybenzene*).

$(CH_3)_2C_6H_3(OH)$. $C_8H_{10}O$. 122.

10 gms. of dimethylcyclohexenone (p. 82) are dissolved in 20 gms. of glacial acetic acid, and the solution cooled by ice-water, care being taken that the acid does not solidify. A solution of 13 gms. of bromine in 10 gms. of glacial acetic acid is added slowly from a dropping funnel with stirring, and the whole allowed to stand overnight in a draught cupboard; hydrobromic acid is evolved. Next day the solution is heated on a water bath to about 50° with frequent shaking; after being a short time at this temperature the bath is raised to boiling, and heating continued until there is but slight evolution of hydrobromic acid. A reflux air condenser is then attached and heating continued over a wire gauze until the acetic acid commences to boil, and until the evolution of hydrobromic acid almost ceases. The solution is cooled and poured into a cold solution of 75 gms. of caustic potash in 150 c.cs. of water. The by-products insoluble in the potash solution are extracted with ether, and the alkaline solution saturated with carbon dioxide to liberate the xylenol, which is distilled off in steam in presence of carbon dioxide. The distillation is stopped when a test portion of the distillate gives no precipitate of tribromo-xylenol (see p. 353) on the addition of a few drops of bromine. The distillate is left in the ice chest overnight, when the greater part of the xylenol crystallises out; this is filtered off. The xylenol in the filtrate is recovered by saturating with common salt and extracting with ether.



*Yield.*—60% theoretical (6 gms.). Crystalline substance; M.P. 64°; B.P. $^{760}$ 220°—221°. (Bl., [3], 11, 702; B., 18, 362, 2672; 20, 410.)

PREPARATION 447.—**Glutaric Acid** [*Pentan di-acid*].

$$COOH.CH_2.CH_2.CH_2.COOH. \quad C_5H_8O_4. \quad 132.$$

A mixture of 20 gms. methylenedimalonic ester (p. 144), 20 gms. conc. hydrochloric acid and 20 c.cs. of water is heated for 6 hours in a flask under reflux. At the end of this time the product is evaporated to dryness, and the residue (glutaric acid) distilled under reduced pressure; it distils at 185°—195° under 10 mms. pressure. The small quantity of anhydride formed is eliminated by warming with a little water. After drying, the product is recrystallised from benzene.

$$CH_2\{CH(COOC_2H_5)_2\}_2 \rightarrow COOH.CH_2.CH_2.CH_2.COOH + 4C_2H_5OH + 2CO_2.$$

*Yield.*—75% theoretical (6 gms.). Soluble in hot benzene; M.P. 97°. (B., 27, 2346; O. S., V., 69; X., 58.)

PREPARATION 448.—**2 : 6-Dibromoaniline** (2 : 6-*Dibromo*-1-*amino-benzene*).

$$C_6H_3(NH_2)Br_2. \quad C_6H_5NBr_2. \quad 251.$$

45 gms. of conc. sulphuric acid, 13 c.cs. of water and 10 gms. of dry dibromosulphanilic acid (p. 348) are placed in a flask, which is fitted with a cork bored with three holes. Through one hole a glass tube, sealed at the lower end and passing down into the mixture, is inserted; inside this tube a thermometer is placed. The other holes hold glass tubes to convey superheated steam through the flask. The mixture is heated to 170° in an oil bath, and superheated steam is blown through. The temperature rises gradually, but must not be allowed to exceed 180°. Some of the dibromoaniline formed is carried over by the steam, but most of it remains in the flask. After about 90 minutes, steam is shut off and the contents of the flask poured into a large volume of cold water. The precipitate is filtered off, dried on filter paper, and recrystallised from petroleum ether.

$$NH_2.C_6H_2Br_2SO_3H + H_2O \rightarrow NH_2C_6H_3Br_2 + H_2SO_4.$$

*Yield.*—83% theoretical (6 gms.). Colourless needles; M.P. 83°—84°. (A., 253, 275.)

PREPARATION 449.—**Benzenesulphinic Acid.**

$$C_6H_5.SO_2H. \quad C_6H_6O_2S. \quad 142.$$

40 c.cs. water are placed in a 300-c.c. flask provided with a reflux condenser and dropping funnel and heated to boiling. 10 gms. of good quality zinc dust are added, the source of heat is withdrawn, and 10 gms. of benzenesulphonic chloride, in small portions at a time, are added from the funnel. A vigorous reaction follows each addition, and this is allowed to subside before more is added. When all is in, the flask is heated for a short time over a small flame, then cooled, and the precipitate of zinc dust and zinc benzenesulphinate filtered off. The precipitate is then mixed with a solution of 10 gms. anhydrous sodium carbonate in 50 c.cs.

of water, and the whole heated for 10 minutes on a boiling water bath; by this means sodium benzenesulphinate is formed and goes into solution. The precipitate is filtered off. The filtrate is evaporated to half its volume, then cooled and acidified with dilute sulphuric acid. Scratching the sides of the containing vessel with a glass rod induces colourless crystals of benzenesulphinic acid to separate after a time. These are filtered off and recrystallised from a little water.

$$2C_6H_5SO_2.Cl + 2Zn \longrightarrow (C_6H_5SO_2)_2Zn + ZnCl_2.$$

Colourless crystals; insoluble in water; M.P. 83°—84°. (B., 9, 1585; O. S., II., 89.)

PREPARATION 450.—**Allyl Alcohol.**

$$CH_2 : CH.CH_2OH. \qquad C_3H_6O. \qquad 58.$$

*This preparation must be conducted in a fume cupboard.*

400 gms. of glycerol (excess), 100 gms. oxalic acid, and 0·5 gms. ammonium chloride are heated in a retort with condenser and receiver attached. The heating is carried out on a wire gauze, and a thermometer is inserted in the liquid. Carbon dioxide is rapidly evolved at first, and the temperature remains about 130°. The evolution of gas slackens as the temperature gradually increases to about 180° and then ceases. At 195° the receiver containing aqueous formic acid is changed, and at 200°—210° carbon dioxide is again evolved, and oil condenses in neck of retort. The temperature is raised to 220°—230° and maintained there for some time, being finally raised to 260°, at which temperature distillation is stopped. The residue in the flask consists of glycerol to which more oxalic acid may be added and the process repeated. The distillate containing allyl alcohol is again distilled until no oil separates from a sample of the distillate on treating with solid potassium carbonate, which takes place when the temperature reaches about 105°. The allyl alcohol is separated from the distillate by adding solid potassium carbonate, and distilled, the fraction boiling at 93°—97° being collected.

$$C_3H_5(OH)_3 \longrightarrow C_3H_5(OH)_2O.CO.COOH \longrightarrow C_3H_5(OH)_2O.COH \longrightarrow$$
$$CH_2 : CHCH_2OH + CO_2 + H_2O.$$

*Yield.*—30 gms.; B.P. 96°; D° 0·87. (A., 156, 129; O. S., I., 15.)

# CHAPTER XXXII

## MISCELLANEOUS PREPARATIONS

Preparation 451.—**Benzoyl Peroxide.**

$$C_6H_5CO.O.O.CO.C_6H_5. \qquad C_{14}H_{10}O_4. \qquad 242.$$

50 c.cs. of 10% hydrogen peroxide are placed in a glass-stoppered flask surrounded by a good cooling mixture. 4N-caustic soda solution and benzoyl chloride are dropped in alternately, with continual shaking, so that the solution remains weakly alkaline. The hydrogen peroxide is decomposed when 30 c.cs. of caustic soda solution and 15 gms. of benzoyl chloride have been added. The benzoyl peroxide separates in crystalline flocks, is filtered, washed with water, and crystallised from a small quantity of boiling alcohol.

*Yield.*—80—95% theoretical (10—12 gms.); colourless prisms; M.P. 106°—108°, with decomposition.

By the action of sodium ethoxide in absolute ether, it is decomposed into sodium perbenzoate and benzoic ester :—

$$C_6H_5.\underset{\ddot{O}}{C}.O.O.\underset{\ddot{O}}{C}.C_6H_5 \longrightarrow C_6H_5.\underset{\ddot{O}}{C}OONa + C_2H_5O.\underset{\ddot{O}}{C}.C_6H_5.$$

Perbenzoic acid (M.P. 41°—43°) can be obtained by extracting with chloroform after acidification. (B., 27, 1510; 33, 1575).

It is used as an oxidising and a benzoylating agent. (G., 60, 859; J. pr., 128, (ii.), 171.)

Many aliphatic and aromatic acids yield similar derivatives.

Preparation 452.—**Cupferron ($NH_4$ salt of nitrosophenylhydroxylamine).**

$$C_6H_5N\!\left\langle\begin{array}{l}NO\\ ONH_4.\end{array}\right. \qquad C_6H_9O_2N_3. \qquad 155.$$

725 gms. phenylhydroxylamine, obtained from the reduction of nitrobenzene (see Preparation 376), are treated with 3 litres ether. The ether insoluble material (sodium chloride) is filtered off and weighed, this weight being deducted from the weight of crude phenylhydroxylamine. The filtrate is placed in a 5-litre round-bottomed flask, cooled to 0°, and stirred with an efficient mechanical stirrer, while a rapid stream of ammonia gas is passed into the solution. After about 15 minutes the theoretical quantity of freshly distilled amyl nitrite (107 gms. for each 100 gms. phenylhydroxylamine) is added through a dropping funnel. The addition of amyl nitrite requires about 30 minutes, during which time the stream of ammonia is continued, so that ammonia will remain in excess (otherwise

a coloured product results). The temperature should not exceed 10° during this addition. After the addition of the nitrite the mixture is stirred for 10 minutes to ensure complete reaction. The cupferron is then filtered off, washed several times with ether, and dried by exposure on sheets of filter paper. It is stored in a bottle, where it is exposed to the vapours of ammonia: this is effected by placing a small tube containing solid ammonium carbonate, and which is drawn out to a fine capillary, inside the bottle of cupferron.

$$C_6H_5NHOH \rightarrow C_6H_5N\begin{matrix}\diagup NO\\ \diagdown ONH_4\end{matrix} \quad \text{or } C_6H_5N\begin{matrix}\diagup\!\!\diagup O\\ \diagdown NO.NH_4.\end{matrix}$$

*Yield.*—80—90% theoretical (800 gms.). (O. S., IV., 19.)

This reagent is much used for the estimation of copper and iron (hence its name). See text-books on inorganic analysis. (Am. Soc., 41, 276.)

PREPARATION 453.—**Benzenesulphonyl Chloride.**

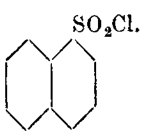
$C_6H_5SO_2Cl$. 176·5.

150 gms. of sodium benzene sulphonate, which have been dried for 3 hours at 140°, are mixed with 85 gms. of finely divided phosphorus pentachloride in a round-bottomed flask provided with a reflux condenser. The mixture is heated at 170°—180° in an oil bath. The flask should be removed every 4 hours, stoppered, and vigorously shaken until the mass becomes pasty. The mass is poured into a mixture of ice and water, when the benzene sulphonyl chloride sinks to the bottom; it is separated, washed with water, and distilled *in vacuo*, the fraction 113°—115° at 10 mms. being collected. The phosphorus pentachloride may be replaced by 100 gms. phosphorus oxychloride.

$$3C_6H_5SO_2.ONa + PCl_5 = 3C_6H_5SO_2Cl + 2NaCl + NaPO_3.$$
$$2C_6H_5SO_2.ONa + POCl_3 = 2C_6H_5SO_2Cl + NaCl + NaPO_3.$$

*Yield.*—75—80% theoretical (110—120 gms.). Colourless oil; M.P. 14·5°; B.P. $^{760}$ 246° (decomposition). (B., 42, 1802, 2057; O. S., I., 21; X., 6.)

PREPARATION 454.—**α-Naphthalenesulphonyl Chloride.**




$C_{18}H_7O_2ClS$ 226·5.

30 gms. (1 mol.) of sodium α-naphthalene sulphonate previously dried at 150° are gradually added while warm to 30 gms. (slight excess) of phosphorus pentachloride contained in a basin or beaker. The reaction commences on the addition of the first portions, and further addition is regulated so that the reaction does not become too vigorous. After the final addition the whole is heated on a water bath until homogeneous. Afterwards it is transferred to a flask and distilled under reduced pressure until the distillate—which consists at first of phosphorus oxychloride—

weighs 15—20 gms. The residue in the flask is poured into a mortar and stirred as it solidifies; when solid it is mixed with ice-water, ground up and filtered. It is then well pressed for a short time on a porous plate, and after complete drying, *in vacuo*, over sulphuric acid, is recrystallised from a mixture of benzene and petroleum ether.

$$C_{10}H_7SO_2OH + PCl_5 \longrightarrow C_{10}H_7SO_2Cl + HCl + POCl_3.$$

*Yield.*—60% theoretical (17·5 gms.). M.P. 66°.

*β-Naphthalene sulphonyl chloride* is prepared in a similar manner from sodium β-naphthalene sulphonate. (A., 275, 233.)

PREPARATION 455.—**Ethyl Potassium Sulphate.**

$C_2H_5O.SO_3K$. $C_2H_5O_4SK$. 164.

To 100 c.cs. ethyl alcohol in a ½-litre round-bottomed flask are carefully added with cooling 40 c.cs. conc. sulphuric acid. A reflux condenser is attached and the mixture heated for an hour on the water bath, and then allowed to cool. The liquid is poured into ½ litre of water in a porcelain basin, and to this is added chalk, with stirring, until effervescence ceases. The calcium sulphate is filtered off, and washed with a little warm water. To the filtrate, which contains ethyl calcium sulphate, is added saturated potassium carbonate solution until the liquid gives a faint alkaline reaction to phenolphthalein. The calcium carbonate is filtered off and washed with a little hot water. The filtrate is then evaporated until crystallisation begins, when it is set aside to cool. The crystals of ethyl potassium sulphate are filtered off and dried, and a further crop obtained by concentrating the mother liquor.

$$C_2H_5OH + H_2SO_4 \longrightarrow C_2H_5O.SO_3H \longrightarrow (C_2H_5O.SO_3)_2Ca \longrightarrow C_2H_5O.SO_3K.$$

*Yield.*—15% theoretical (45 gms.). Deliquescent, monoclinic plates; soluble in water; insoluble in alcohol or ether. (Bl., 19, 295.)

PREPARATION 456.—**Aminoazobenzene.**

$C_6H_5N:N.C_6H_4NH_2$. $C_{12}H_{11}N_3$. 197.

10 gms. of finely ground diazoaminobenzene, 5 gms. of aniline hydrochloride, and 20 gms. of aniline are heated in a beaker at 40° for an hour. After standing overnight at ordinary temperature, the mixture is treated with an excess of dilute acetic acid to dissolve the aniline; aminoazobenzene remains undissolved. It is filtered off, washed with water, and recrystallised from dilute alcohol.

$$C_6H_5N:N.NH.C_6H_5 \longrightarrow C_6H_5N:N.C_6H_4NH_2.$$

*Yield.*—80% theoretical (8 gms.). Yellow needles; M.P. 126°; stable basic substance. (B., 19, 1953; 20, 372.)

PREPARATION 457.—**Nitrosobenzene.**

$C_6H_5NO$. 107.

4·6 gms. potassium dichromate (or an equivalent quantity of sodium dichromate) are dissolved in 200 c.cs. water and the solution cooled to 0° in a freezing mixture. A mixture containing 4 gms. finely powdered

phenylhydroxylamine, 30 gms. conc. sulphuric acid, and 270 c.cs. of water is also cooled in ice-water, and to it the dichromate solution is added quickly. The nitrosobenzene which separates is removed by steam distillation, and if any solidifies in the condenser the water should be run out of the latter until the solid melts and flows down into the receiver. The nitrosobenzene is filtered off from the distillate, pressed on a porous plate until dry, and washed with a little petroleum ether.

$$C_6H_5NH.OH + O \rightarrow C_6H_5NO + H_2O.$$

M.P. 68° ; colourless or yellow crystals. (D.R.P., 89978 ; 105875.)

PREPARATION 458.—**Aniline Nitrate** (*Phenylammonium nitrate*).

$$C_6H_5NH_3.NO_3. \qquad C_6H_8O_3N_2. \qquad 156.$$

**Aniline Hydrochloride** (*Phenylammonium chloride*).

$$C_6H_5NH_3.Cl. \qquad C_6H_8NCl. \qquad 129{\cdot}5.$$

The preparation of aniline nitrate is fully described on p. 375 under the preparation of diazobenzene nitrate. The crude product therein obtained is recrystallised by dissolving in a little absolute alcohol and precipitating therefrom with ether. The preparation and purification of aniline hydrochloride are exactly similar.

$$C_6H_5NH_2 + HNO_3 = C_6H_5NH_3.NO_3.$$
$$C_6H_5NH_2 + HCl = C_6H_5NH_3.Cl.$$

*Yields.—Aniline Nitrate.*—80% theoretical (13 gms. from 10 gms. of aniline). *Aniline Hydrochloride.*—80% theoretical (10 gms. from 10 gms. of aniline). Colourless crystals ; soluble in water and alcohol ; insoluble in ether ; aniline hydrochloride melts at 198° ; aniline nitrate transforms to nitroaniline at 190°. (A. Ch., [6], 21, 355 ; J., 1861, 495 ; B., 14, 1083.)

**Aniline Sulphate.**

$$(C_6H_5NH_3)_2SO_4. \qquad C_{12}H_{16}O_4N_2S. \qquad 284.$$

To 10 gms. (2 mols.) of aniline 15 c.cs. (an excess) of dilute (5N) sulphuric acid are added. The precipitate is recrystallised from a little water.

$$2C_6H_5NH_2 + H_2SO_4 = (C_6H_5NH_3)_2SO_4.$$

*Yield.*—90% theoretical (13·5 gms.). Colourless crystals ; soluble in water ; slightly soluble in absolute alcohol ; insoluble in ether. (A. Ch., [6], 21, 355 ; B., 18, 3313.)

PREPARATION 459.—**Aniline Hydroferrocyanide** (*Phenylammonium ferrocyanide*).

Aniline is dissolved in conc. hydrochloric acid until only slightly acid. Water is then added until the whole is a saturated solution of aniline hydrochloride at ordinary temperature. A saturated solution of sodium ferrocyanide is then added until precipitation is complete. The solution should be slightly acid after this stage has been reached. The white precipitate is filtered off, washed first with a little alcohol and then ether, and dried by suction.

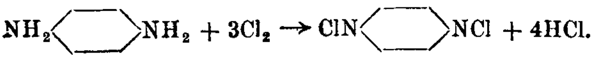
$$2C_6H_5NH_2 + H_4Fe(CN)_6 \rightarrow 2C_6H_5NH_2.H_4Fe(CN)_6[.2H_2O].$$

*Yield.*—Theoretical. White rhombohedral crystals with greenish tinge; infusible; almost insoluble in water, solution being decomposed on boiling with evolution of hydrocyanic acid; insoluble in alcohol or in ether. Many other aromatic organic bases yield similar compounds. (J. C. S., 121, 1293.)

PREPARATION 460.—***p*-Benzoquinone Dichlorimide.**

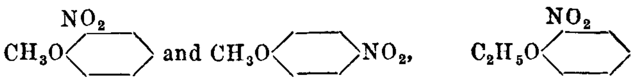
 $C_6H_4N_2Cl_2$. 175.

Chlorine is passed into 250 c.cs. water containing 45 gms. caustic soda until the total weight is 332 gms. 750 c.cs. of ice-water are then added. A solution prepared from commercial sodium hypochlorite (p. 512) may be employed. Into the cold solution are slowly run 27 gms. *p*-phenylenediamine hydrochloride in 300 c.cs. of water and 60 c.cs. of conc. hydrochloric acid. After the blue colour disappears the dichlorimide separates, is filtered and washed with water until the filtrate is free from chlorine; it is then recrystallised from 70% alcohol or petroleum ether (40°—60°).



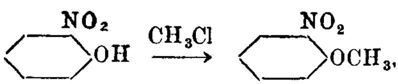
Colourless needles, which explode at 126° (*caution!*). (B., 12, 47.)

PREPARATION 461. — **Alkyl Nitrophenols** (1-*Methoxy*-2-*nitrobenzene, etc.*).

 etc.

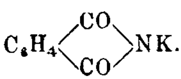
*o*-Nitro-anisole. *o*-Nitro-phenetole.

70 gms. of *ortho*- or *para*-nitrophenol, 20 gms. caustic soda, and 40 gms. sodium carbonate are dissolved in 200 c.cs. water. To this solution are added 250 c.cs. methyl (or ethyl) alcohol, 90%, and the whole cooled to 10° and placed in an autoclave. 1·75 mols. of methyl or ethyl chloride (both are gases at ordinary temperature) are then added, and the temperature is raised to 100° for 8 hours—the pressure being 4—5 atms. The product is poured into water and the alkyl ether separated. The alcohol is then recovered. The alkyl compound is washed with a little caustic soda solution to remove free nitrophenol. It is purified by distillation.



*Yield.*—75—80% theoretical. *o*-Nitroanisole: M.P. 9°; B.P. 265°; *p*-nitroanisole: M.P. 54°; B.P. 258°. *o*-Nitrophenetole: M.P. 78°; B.P. 268°; *p*-nitrophenetole: M.P. 60°; B.P. 283°.

PREPARATION 462.—**Potassium Phthalimide.**

 $C_8H_4O_2NK$. 185.

2·4 gms. phthalimide (previously dried in a steam oven) are dissolved in 80 c.cs. ethyl alcohol (distilled from lime), the solution is heated to boiling, and a hot solution of 1 gm. ($1\frac{1}{2}$ atoms) of potassium in 30 c.cs. of ethyl alcohol added. [The potassium ethoxide is prepared by dissolving the potassium in alcohol, diluted with dry ether, which is afterwards driven off when the solution is raised to boiling on a water bath.] When cold, the white precipitate is filtered off, washed with dry ether, and dried in an oven.

*Yield.*—68% theoretical (2 gms.).

Sodium phthalimide may be prepared in a similar manner, the yield being 50% theoretical.

By using amyl alcohol in place of ethyl alcohol the yields may be improved to above 90% theoretical. (J. C. S., 121, 2362; A., 215, 181.)

PREPARATION 463.—**Phenylhydrazone of *d*-Mannose** (+ + + + *Pentolhexanal*).

$$CH_2(OH)(CH(OH))_4CH : NNH.C_6H_5. \qquad C_{12}H_{18}O_5N_2. \qquad 270.$$

To 4 gms. (1 mol.) of mannitol dissolved in 20 c.cs. of water, a solution of 1 gm. of ferrous sulphate in cold water is added, and then gradually 12 c.cs. (1 atom of O) of hydrogen peroxide solution (20 vols.), or more if solution is weaker, are dropped in. The solution must be well cooled throughout. Sodium carbonate solution is added till just alkaline, the whole filtered, and portions of the filtrate tested for mannose by Fehling's solution, and by ammoniacal silver nitrate. To the bulk of the filtrate 1 c.c (excess) of phenylhydrazine dissolved in a slight excess of dilute acetic acid is added, the solution allowed to stand, and the precipitate of mannose phenylhydrazone filtered off. It is recrystallised from dilute alcohol.

$$CH_2OH(CHOH)_4CH_2OH + O = CH_2OH(CHOH)_4CHO + H_2O.$$

Yellow crystals; M.P. 198°.

PREPARATION 464.—**Diphenyl Disulphide.**

$$C_6H_5S.SC_6H_5. \qquad C_{12}H_{10}S_2. \qquad 218.$$

0·5 c.c. (2 mols.) of thiophenol are dissolved in alcohol, 0·5 c.c. of conc. ammonia added, and the whole evaporated to dryness on a water bath in a good fume cupboard.

$$2C_6H_5SH + O = C_6H_5S.SC_6H_5 + H_2O.$$

*Yield.*—Theoretical. Colourless needles; M.P. 61°.

**Iodobenzene and some Related Compounds.**—Aromatic iodo-compounds containing iodine in the nucleus unite with two atoms of chlorine to form iodochlorides (Preparation 469), the iodine becoming trivalent. Caustic soda converts the latter into iodoso-compounds, oxygen replacing the two chlorine atoms (Preparation 465.)

$$C_6H_5I \longrightarrow C_6H_5ICl_2 \longrightarrow C_6H_5IO.$$

Iodoso-compounds behave as diacid bases, *e.g.*, $C_6H_5I(OH)_2$, which combine with acids to form salts (Preparation 466). Reducing agents or

the action of heat convert them into iodo-compounds, while oxidising agents yield iodoxy-compounds (Preparation 467).

PREPARATION 465.—**Iodosobenzene.**

$$C_6H_5.I:O. \qquad C_6H_5OI. \qquad 220.$$

*By-product.*—**Diphenyliodonium Iodide.**

$$(C_6H_5)_2:I.I. \qquad C_{12}H_{10}I_2. \qquad 408.$$

10 gms. of phenyliodide dichloride (p. 430) are carefully rubbed with a solution of 5 gms. of sodium hydroxide in 40 gms. of water in a mortar and allowed to stand overnight. The iodosobenzene is filtered off, washed with water, and pressed on a porous plate. The alkaline filtrate is saturated with sulphur dioxide, and the precipitated diphenyliodonium iodide crystallised from a small quantity of hot water, or from alcohol.

$$\begin{aligned} C_6H_5I:Cl_2 + 2H_2O &= C_6H_5I(OH)_2 + 2HCl \\ &= C_6H_5.I:O + H_2O + 2HCl. \end{aligned}$$

A small portion of the iodosobenzene is probably oxidised to iodoxybenzene, $C_6H_5IO_2$, which reacts with the hypothetical hydroxide, $C_6H_5.I(OH)_2$, to give diphenyl iodonium hydroxide and iodic acid. This base is present in the alkaline filtrate from the iodosobenzene. The sulphur dioxide reduces the iodic acid to hydriodic acid, which, combining with the iodonium base, forms an iodide insoluble in cold water.

$$C_6H_5.I\begin{matrix}\diagup OH \\ \diagdown OH\end{matrix} + IO_2C_6H_5 = C_6H_5.I(OH).C_6H_5 + HIO_3.$$

$$HIO_3 + 3SO_2 + 3H_2O = HI + 3H_2SO_4.$$

$$(C_6H_5)_2I.OH + HI = (C_6H_5)_2I.I + H_2O.$$

*Yields.—Iodosobenzene.*—75% theoretical (6 gms.). White amorphous substance; soluble in water, yielding a neutral solution; decomposes when heated to above 240°.

*Diphenyliodonium Iodide.*—Crystallises from alcohol in long, yellow needles: M.P. 175°—176°; on melting decomposes completely into iodobenzene. (B., 25, 3495; 26, 1307, 1354; 27, 506.)

PREPARATION 466.—**Iodosobenzene Acetate.**

$$C_6H_5I:(O.CO.CH_3)_2. \qquad C_{10}H_{11}O_4I. \qquad 322.$$

5 gms. (1 mol.) of iodosobenzene are dissolved with heat in the smallest possible quantity of glacial acetic acid, the solution evaporated to dryness on a water bath, and the powdered residue recrystallised from a little benzene.

$$C_6H_5I:O + 2CH_3COOH = C_6H_5I:(O.CO.CH_3)_2 + H_2O.$$

*Yield.*—Theoretical (7 gms.). Colourless prisms; M.P. 156°—157°.

PREPARATION 467.—**Iodoxybenzene** (*Phenyl iodite*).

$$C_6H_5.IO_2. \qquad C_6H_5O_2I. \qquad 236.$$

10 gms. (1 mol.) of iodosobenzene are mixed in a flask with sufficient water to form a thin paste, and steam distilled until no more iodobenzene

comes over, and until all the iodosobenzene has completely reacted. If the iodoxybenzene formed does not dissolve completely, water is added until solution takes place. The residue is then filtered and concentrated on a water bath until a test portion, on cooling, gives a copious precipitate.

$$2C_6H_5I : O = C_6H_5IO_2 + C_6H_5I.$$

Snow-white powder; decomposes suddenly on heating to 210°—230°.

PREPARATION 468.—**Diphenyliodonium Iodide.**

$$(C_6H_5)_2I.I. \qquad C_{12}H_{10}I_2. \qquad 408.$$

10 gms. (1 mol.) of iodosobenzene and 11 gms. (1 mol.) of iodoxybenzene are treated with water and with 20 gms. (excess) of freshly precipitated silver oxide in a stout, well-stoppered bottle, shaken mechanically for 4 hours, and filtered. The filtrate, which contains free diphenyliodonium hydroxide, has a strongly alkaline reaction.* The base has not been obtained in a pure form, but its salts are readily prepared from the solution.

The solution contains part of the base in the form of its iodate, and is therefore first treated with sulphur dioxide, and then with excess of potassium iodide solution, when the iodide separates out completely. It is recrystallised from alcohol.

$$C_6H_5I : O + C_6H_5IO_2 + AgOH \longrightarrow (C_6H_5)_2I.OH + AgIO_2.$$
$$(C_6H_5)_2I.OH + KI \longrightarrow (C_6H_5)_2I.I.$$

*Yield.*—93% theoretical (17 gms.). Yellow needles from alcohol; M.P. 175°—176°; on melting decomposes completely into iodobenzene. (B., 27, 426; 502, 1592.)

PREPARATION 469.—**Phenyliodide Dichloride.**

$$C_6H_5.I : Cl_2. \qquad C_6H_5Cl_2I. \qquad 275.$$

10 gms. (1 mol.) of iodobenzene are dissolved in 20 c.cs. of dry chloroform, and a current of chlorine, dried by bubbling through two concentrated sulphuric acid wash-bottles, is led into the solution through a *very wide* delivery tube. During the passage of the gas the solution is cooled by ice-water; when no more gas is absorbed the yellow crystals are filtered off, washed with chloroform, spread out in a thin layer on a pad of filter paper, and allowed to dry in the air.

$$C_6H_5I + Cl_2 = C_6H_5I : Cl_2.$$

*Yield.*—Almost theoretical (13 gms.). Very unstable yellow crystals; decompose on heating. (J. pr., 33, 154; B., 26, 357; A., 369, 119.)

PREPARATION 470.—**β-Naphthalenesulphonylglycine.**

$$C_{10}H_7.SO_2.NH.CH_2.COOH. \qquad C_{12}H_{11}O_4NS. \qquad 265.$$

2 gms. (1 mol.) of glycocoll are dissolved in 27 c.cs. (1 mol.) of normal sodium hydroxide, and to this an ethereal solution of 12 gms. (2 mols.) of β-naphthalene-sulphonyl chloride is added. The mixture is shaken in a stoppered bottle in a shaking machine at ordinary temperature. Three

* Test solution for an iodate.

times, at intervals of about an hour, the same amount of normal alkali is again added. After about 4 hours the aqueous liquid, which still reacts alkaline, is separated from the ethereal layer in a funnel, filtered, and acidified with hydrochloric acid. The oil which is precipitated soon crystallises. For complete purification it is recrystallised from hot water.

$$C_{10}H_7.SO_2Cl + NH_2.CH_2.COOH = C_{10}H_7SO_2.NHCH_2.COOH + HCl.$$

Colourless laminæ, M.P. 156° (159° corr.). (B., 35, 3780.)

PREPARATION 471.—**Thiophenol.**

$C_6H_5SH$. $C_6H_6S$. 110.

This experiment should be performed in a good draught chamber. 240 gms. conc. sulphuric acid and 720 gms. crushed ice are placed in a litre round-bottomed flask. The mixture is cooled by placing the flask in a freezing mixture; the temperature should be kept below 0°. Stirring is commenced, and 60 gms. benzene sulphonyl chloride (see p. 424) are gradually run in during ½ hour. 120 gms. of zinc dust are then added as quickly as possible without allowing the temperature to rise above 0°; this requires about ½ hour. The stirring is continued for 1—1½ hours, the temperature being kept below 0°. A reflux condenser is now attached, the freezing bath is removed, and the temperature allowed to rise spontaneously or by the application of a little heat, the agitation being maintained. A vigorous action ensues after a time, and much hydrogen is evolved, at which stage cooling should be applied. The mixture is then heated to boiling until the solution becomes clear (about 4—7 hours). The thiophenol is steam distilled, separated from the water, and dried with calcium chloride. It is distilled, the fraction boiling at 166°—175° (71° at 15 mms.) is collected.

$$C_6H_5SO_2Cl + 6H \longrightarrow C_6H_5SH + 2H_2O + HCl.$$

*Yield.*—90% theoretical (34 gms.). Colourless liquid; B.P. 173°; characteristic unpleasant odour; produces burns on the skin; vapour irritates the eyes. (A., 119, 142; B., 28, 2319; 51, 751; O. S., I., 71.)

PREPARATION 472.—**Lead and Mercury Salts of Thiophenol.**

$(C_6H_5S)_2Pb$. $(C_6H_5S)_2Hg$.
$C_{12}H_{10}S_2Pb$. 425. $C_{12}H_{10}S_2Hg$. 418.

1 gm. (excess) of lead acetate or mercuric chloride is dissolved in alcohol by the application of heat, and the solution cooled and filtered. 0·5 c.c. (2 mols.) of thiophenol is then added drop by drop when a precipitate of the required salt is obtained. It is washed with a little alcohol.

$$2C_6H_5SH + (CH_3COO)_2Pb = (C_6H_5S)_2Pb + 2CH_3.COOH.$$
$$2C_6H_5SH + HgCl_2 = (C_6H_5S)_2Hg + 2HCl.$$

*Yield.*—Theoretical (1 gm.). Crystalline substances; insoluble in alcohol.

PREPARATION 473.—**Lead and Calcium Salts of Glyceric Acid.**

$(Pb \text{ or } Ca)[O.CO.CH(OH)CH_2OH]_2$.

*Pb Salt.*—A dilute aqueous solution of glyceric acid (p. 249) is neutralised with lead carbonate containing a small quantity of lead oxide. The

mixture is heated to boiling and filtered hot. The filtrate, on concentrating and cooling, yields the required salt in crusts, which adhere to the sides of the vessel. A further crop may be obtained by concentrating and cooling the mother liquors. The product may be recrystallised from hot water.

*Yield.*—Theoretical (twice the weight of acid taken).

*Ca Salt.*—A dilute aqueous solution of glyceric acid is boiled with excess of calcium carbonate and filtered hot. The filtrate, on concentrating and cooling, yields colourless crystals of the required salt, which may be recrystallised from hot water. (A., 120, 226.)

PREPARATION 474.—**Triphenylchloromethane** (*Triphenylmethyl chloride*).

$$(C_6H_5)_3CCl. \qquad C_{19}H_{15}Cl. \qquad 278{\cdot}5.$$

12·5 gms. of freshly prepared, finely divided anhydrous aluminium chloride (see p. 506) are added in 4 equal portions to a mixture of 10 gms. (1 mol.) of redistilled carbon tetrachloride, which has stood for 48 hours over calcium chloride, and 35 gms. (excess) of pure similarly treated benzene, in a flask fitted with a long reflux condenser. When the reaction moderates, it is completed by heating on a water bath for 1 hour. On cooling, the contents of the flask are very slowly poured with mechanical stirring on to ice surrounded by a freezing mixture. Three times during the addition benzene is added, sufficient to dissolve the triphenylchloromethane as it separates. The benzene solution is separated, washed with dilute hydrochloric acid, then with water, dried over calcium chloride, and evaporated on a water bath until triphenylchloromethane crystallises on cooling a sample. After filtration, a further yield may be obtained by removing the benzene under reduced pressure at 40°, and washing the residue with ether. The whole is purified by retreatment with benzene, as above.

$$3C_6H_6 + CCl_4 \rightarrow ClC(C_6H_5)_3 + 3HCl.$$

*Yield.*—80% theoretical (14 gms.). Colourless crystals; somewhat soluble in benzene; M.P. 111°. (A., 194, 253.)

PREPARATION 475.—**Thianthren** (*Diphenylene disulphide*).

$$C_6H_4{<}^{S}_{S}{>}C_6H_4. \qquad C_{12}H_8S_2. \qquad 216.$$

To the catalyst prepared as described on p. 61, from 25 gms. of aluminium powder, 45 gms. of mercuric chloride and 25 gms. (excess) of pure dry benzene, 10 gms. (4 atoms) of flowers of sulphur are added under good mechanical stirring, and the mixture heated on a water bath until hydrogen sulphide is no longer evolved. The product, on cooling, is decomposed by adding ice, filtered, and the residue repeatedly extracted with chloroform from which the thianthren is obtained on concentration. It is recrystallised from acetone.

$$2C_6H + 4S \xrightarrow{AlCl_3HgCl} C_6H_4{<}^{S}_{S}{>}C_6H_4 + 2H_2S.$$

*Yield.*—80% theoretical (14 gms.). Colourless crystals; soluble in chloroform; insoluble in cold acetone; M.P. 160°. (J. C. S., 117, 1335.)
This is an extension of the Friedel-Craft's Reaction (see p. 58).

### Reactions of Unsaturated Hydrocarbons to Yield Oxy and Other Compounds

Developments in the production of acetaldehyde from acetylene have focussed attention on this reaction. Alcohols may also be formed from olefines. Sulphuric acid (20—45%), phosphoric acid 30—35%), or acetic acid (96%), in presence of a mercury salt may be employed. Selenium dioxide has been used for a similar purpose. (J. C. S., 1932, 2342.) See also, A. C. R., 1934, 123.

With sulphuric acid (55—76%) secondary reactions involving dehydration and polymerisation take place:

$$3C_4H_9OH - 3H_2O \rightarrow (C_4H_8)_3$$

This is an important process for conversion of *iso*-butylene to valuable liquid hydrocarbons. Di- and tri-*iso*butylenes are formed, the relative proportion depending on the concentration of sulphuric acid used. By catalytic reduction they yield *iso*-octane.

PREPARATION 476.—**Acetaldehyde.**

$CH_3.CHO$. $C_2H_4O$. 44.

Acetylene prepared from calcium carbide and purified by passing (1) through copper sulphate solution, and (2) through a tower packed

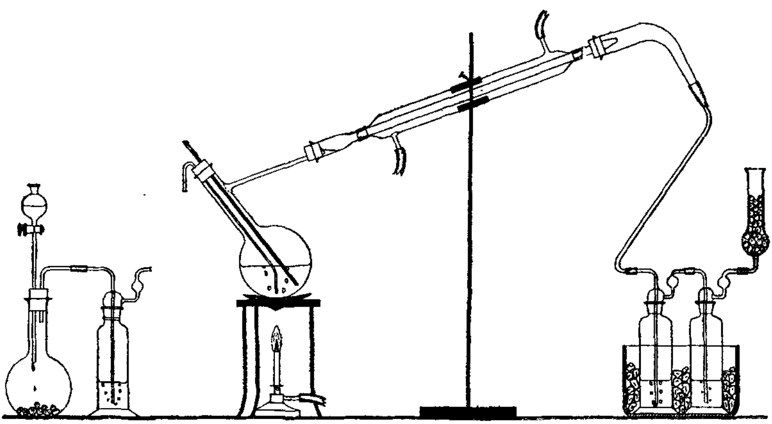


FIG. 57.

with bleaching powder, is led into a flask containing 300 c.cs. of 96% acetic acid and 9·5 gms. mercuric sulphate in solution, the temperature of which is kept at 30° (see Fig. 57). The exit tube from the flask is connected (1) to a cold water condenser, and (2) to two wash-bottles

containing ether and cooled in ice. The gas should be passed at a very moderate rate for 1 or 2 days, and a little water (1—2 c.cs.) added at intervals to replace that taken up in the reaction. When it is decided to discontinue the reaction the flask is warmed to 60°—70° to drive all the aldehyde over into the ether. The ethereal solution is dried over anhydrous sodium sulphate, then decanted, and saturated with dry ammonia. A very good yield of aldehyde-ammonia results.

$$CH \vdots CH + H_2O \rightarrow CH_3.CHO.$$
$$CH_3.CHO + NH_3 \rightarrow CH_3CHOH.NH_2.$$

With more elaborate apparatus involving thorough agitation of the gas with the catalyst, and also a circulatory system by which the escaping acetylene can be repeatedly passed through the catalyst, excellent yields can be obtained. (See Preparation 440.) See also E.P., 373893.

Preparation 477.—**Paracetaldehyde.**

$(CH_3CHO)_3$. $C_6H_{12}O_3$. 132.

A paste, consisting of 10 gms. mercuric sulphate, and 40 gms. of ammonium hydrogen sulphate with 20 c.cs. of water, is introduced into a strong glass bottle of 1,500 c.cs. capacity. The bottle is three-fourths filled with glass beads and thoroughly shaken; it is then fitted with a one-holed cork, carrying a delivery tube, which passes down through the beads. A current of acetylene, prepared from calcium carbide and water, and purified by passing first through copper sulphate solution, and then through a tower packed with bleaching powder, is led into the bottle, which has no outlet and which is periodically shaken.

In about 2 hours the beads adhere together somewhat; then paracetaldehyde begins to collect at the bottom of the bottle. Water is added, 2—3 c.cs. at a time, at intervals during the formation. The yield is good, and there is practically no escape of acetylene or acetaldehyde from the apparatus. The action consists in the formation of a mercuric sulphate acetylene compound and its subsequent decomposition giving paracetaldehyde. The passage of acetylene should be continued for about 2 days. The contents of the bottle are finally shaken up with ether, the ethereal solution separated, dried over anhydrous sodium sulphate, and distilled. Paracetaldehyde passes over as a colourless liquid, boiling point 124°.

$$3C_2H_2 + 3H_2O \rightarrow (CH_3CHO)_3.$$

(Am. Soc., 43, 2071.)

Preparation 478.—**Chloroform** (*Trichloromethane*).

$CHCl_3$. 119·5.

*From Acetone.*—100 gms. of fresh 35% bleaching powder, or an equivalent quantity, are ground up in a mortar to a cream with successive small quantities of water and washed into a 2-litre flask, 400 c.cs. of water being used altogether. (*Note.*—As commercial bleaching powder is variable, the sample should be analysed, and the correct equivalent quantity taken.) 20 gms. acetone are placed in the flask, which is connected to a long condenser and receiver. The flask is gently warmed on a sand bath until a reaction commences, when the flame is withdrawn until the reaction sub-

sides; much frothing takes place at this stage if the reaction is going properly. Heat is again applied and distillation continued so long as any oily drops of chloroform pass over. The distillate is placed in a separating funnel, and the bottom layer of chloroform run off. This is washed with dilute sodium hydroxide, dried over granular calcium chloride and distilled.

*Yield.*—(20 gms.) Colourless liquid; B.P. 61°; D.$^{12}_{4}$ 1·504.

$$CH_2.CO.CH_2 + 3Cl_2 \rightarrow CH_2COC.Cl_3 + 3HCl.$$
$$2CH_2.CO.CCl_2 + Ca(OH)_2 \rightarrow (CH_2COO)_2Ca + 2CHCl_2.$$

*From Alcohol.*—46 gms. of alcohol are treated with chlorine, first below 10° and, when absorption slackens, at 60° until the gas is no longer absorbed. For further details see Preparation 355. The product which contains chiefly chloral alcoholate is transferred, washing out with water, to a large flask which is connected to a long condenser having an attached adapter dipping just under the surface of water in a receiver. 115 gms. of fresh 35% bleaching powder and 20 gms. lime ground up into a paste with water in a mortar are washed into the flask with water, 450 c.cs. of water being used altogether. The method thereafter is the same as described above.

$$CH_2CH_2OH \rightarrow CCl_3CHO \rightarrow CHCl_2 + Ca(OOCH)_2.$$

(D. R. P., 129237 (1902); A., 23, 244; J. Eng., 4, 345, 406.)

PREPARATION 479.—**Iodoform** (*Triiodomethane*).

$CHI_3$. 394.

*From Alcohol.*—To 32 gms. potassium carbonate dissolved in 80 gms. water 16 gms. 95% alcohol are added, and the solution heated to 70°. 32 gms. powdered iodine are added gradually with stirring. Iodoform gradually separates out, and when the solution has become completely decolorised, is filtered off, washed with water, and dried at ordinary temperature. A further yield is obtained by adding 2—3 gms. potassium bichromate and 16—24 gms. conc. hydrochloric acid, neutralising and adding 32 gms. potassium carbonate, 16 gms. 95% alcohol and 6 gms. iodine, and carrying out as before.

The iodoform is then recrystallised from alcohol.

$$C_2H_5OH \rightarrow CI_2CHO \rightarrow CHI_2.$$

(J., 1874, 317.) See also Bl., [3], 1, 4.

*From Acetone.*—10 gms. iodine are dissolved in 32 gms. warm 10% caustic soda solution, and after cooling, 2 gms. of acetone added. 10 gms. powdered iodine are added with stirring and then caustic soda solution gradually, until the iodine disappears. The iodoform separates and is filtered off. 2 gms. acetone are added to the filtrate, which has been acidified with hydrochloric acid, and then made alkaline with caustic soda and a further yield of iodoform obtained.

$$CH_3COCH_3 \rightarrow CH_2COCI_2 \rightarrow CHI_3.$$

Lemon yellow hexagonal crystals; M.P. 115°; characteristic odour; sparingly soluble in water.

(A. Spl., 7, 218, 377.)

PREPARATION 480.—**Thiourea** (*Thiocarbamide*).

$$S:C\begin{matrix}\diagup NH_2 \\ \diagdown NH_2.\end{matrix} \qquad CH_4N_2S. \qquad 76.$$

50 gms. of ammonium thiocyanate are melted in a round-bottomed flask in a paraffin bath and kept at a temperature at which the mass remains just liquid (140°—150°) for 5—6 hours, or at 170° for 1 hour. The former method gives the better yield. The cooled melt is powdered and ground up with half its weight of cold water, which dissolves unchanged ammonium thiocyanate, but little of the thiourea. The residue is recrystallised from hot water.

$$CNS.(NH_4) \rightleftarrows CS(NH_2)_2.$$

*Yield.*—14—16% of complete conversion (7—8 gms.); slightly soluble in cold water (1 in 11); soluble in hot water and alcohol; almost insoluble in ether or benzene; M.P. 172°. (J. C. S., 22, 1; 83, 1; J. pr., [2], 9, 10.)

PREPARATION 481.—**Urea** (*Carbamide*).

$$CO\begin{matrix}\diagup NH_2 \\ \diagdown NH_2.\end{matrix} \qquad CH_4ON_2. \qquad 60.$$

*Volhard's Method.*—39 gms. potassium cyanide and 10 gms. caustic potash are dissolved in 100 c.cs. of water in a large flask. 63 gms. potassium permanganate dissolved in 1 litre of water are then added, drop by drop, from a funnel, the flask being placed in a freezing mixture. The temperature should not rise above 8°. This is filtered, and a solution of 80 gms. ammonium sulphate is added, and the whole evaporated to dryness. The residue is powdered and extracted with 80 c.cs. absolute alcohol under a reflux at boiling point for ½ hour. It is then filtered and the residue washed with boiling alcohol. The alcohol is removed by distillation until the volume is about 50 c.cs. It is then placed in a glass dish and allowed to stand. The crystals which separate are filtered, washed with alcohol, and dried. A second crop of crystals can be obtained from the mother liquor.

*Second Method.*—50 gms. of potassium cyanide are heated in a large iron crucible over a large burner or blowpipe flame until it begins to fuse. 140 gms. of red lead, in small portions at a time, are added while the mixture is stirred with a rod. When the addition is complete and frothing has ceased the fused mass is poured on to an iron tray. When cold, the mass is separated from metallic lead, ground in a mortar, and digested with 200 c.cs. of cold water for an hour. The filtrate from this mixture is treated with 25 gms. of ammonium sulphate and evaporated in a basin to dryness on a water bath. The residue, ground finely and transferred to a flask, is boiled with three instalments of alcohol under reflux to dissolve the urea from the potassium sulphate. Each extract

is decanted or filtered, and the combined extracts are evaporated to small bulk until crystals of urea separate on cooling and standing.

$$KCN \longrightarrow KOCN \longrightarrow NH_4CNO \longrightarrow CO(NH_2)_2.$$

Prisms; M.P. 132°; very soluble in water. (J., 1880, 393.) (For views on structure, see Werner, "The Chemistry of Urea," Longmans, 1923.) For preparation of methylurea, see O.S., XV., 48.

PREPARATION 482.—**Methylamine Hydrochloride.**

$CH_3.NH_2.HCl.$ $CH_6NCl.$ 67·5.

125 gms. ammonium chloride and 250 gms. 40% aqueous formaldehyde solution are placed in a distilling flask with thermometer well below surface of liquor. The flask is attached to a water condenser, and slowly heated until the thermometer registers 104°, at which it is maintained constant until no further liquid distils over. Weight of distillate = 54 gms. The product in the flask is cooled and filtered from ammonium chloride which separates. The filtrate is evaporated on a water bath to half its original volume, cooled and a second crop of ammonium chloride filtered off. The liquid is then concentrated at 100° until a crystalline scum forms on the surface. On cooling, methylamine hydrochloride separates, and is filtered off. After further evaporation and cooling, a second crop of methylamine hydrochloride is similarly obtained. The filtrate is again concentrated, and left for 24 hours over solid caustic soda in a vacuum desiccator; the semi-solid residue is extracted with warm chloroform which dissolves out any dimethylamine hydrochloride, and a further quantity of methylamine hydrochloride is filtered off. The total yield is treated with boiling chloroform, filtered hot, washed with warm chloroform, and dried in a desiccator.

$$H.CHO + NH_3.HCl \longrightarrow H.CH\begin{cases} OH \\ NH_2.HCl \end{cases} \longrightarrow H.CH:NH.HCl + H_2O.$$

$$CH_2:NH.HCl + H_2O + H.CHO \longrightarrow CH_3.NH_2.HCl + HCOOH.$$

*Yield.*—50% theoretical (45 gms.). Large deliquescent plates; insoluble in chloroform. (J. C. S., 111, 844; Am. Soc., 50, 1786; O.S., III., 67.)

PREPARATION 483.—**ββ-Dinaphthylamine.**

$(C_{10}H_7)_2NH.$ $C_{20}H_{15}N.$ 269.

100 gms. of β-naphthylamine and 0·5 gm. of iodine are heated to 230° for 4 hours. The melt is then cooled and recrystallised from benzene.

$$2C_{10}H_7NH_2 \longrightarrow (C_{10}H_7)_2NH + NH_3.$$

*Yield.*—Almost theoretical (92 gms.). Silver glistening plates; M.P. 170·5°; sparingly soluble in hot alcohol; easily soluble in hot glacial acetic acid. (J. pr., [2], 89, 23, 35.)

PREPARATION 484.—**Phenyl-β-naphthylamine.**

$C_{10}H_7NH.C_6H_5.$ $C_{16}H_{13}N.$ 219.

90 gms. of β-naphthol and 112·5 gms. of aniline are heated for 7 hours

to 100°—190° with 1 gm. of iodine. The melt is boiled out first with dilute hydrochloric acid and then with dilute caustic soda. The residue is dried and distilled *in vacuo*. The phenylnaphthylamine passes over at 237° (15 mms.). It is recrystallised from methyl alcohol.

$$C_{10}H_7OH + H_2N.C_6H_5 \rightarrow C_{10}H_7NH.C_6H_5 + H_2O.$$

*Yield.*—Almost theoretical (130 gms.). Needles ; M.P. 108°. (B., 13, 1850.)

PREPARATION 485.—**Thiocarbanilide** (*s-Diphenylthiocarbamide*).

$$CS(NHC_6H_5)_2. \qquad C_{13}H_{12}N_2S. \qquad 228.$$

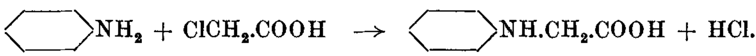
50 gms. carbon disulphide and 40 gms. aniline are dissolved in 60 c.cs. alcohol and 10 gms. powdered caustic potash are added. The whole is heated to boiling (*caution !*) on a water bath for 3—4 hours under a long reflux condenser. (Carbon disulphide boils at 46°.) The carbon disulphide and alcohol are then distilled off, and the residue is washed with water and with dilute hydrochloric acid to remove unchanged aniline. It is then filtered, washed with water, and recrystallised from alcohol.

*Yield.*—70% theoretical (35 gms.). Colourless plates ; M.P. 151° ; sparingly soluble in water. (A., 70, 142 ; B., 33, 2726.)

PREPARATION 486.—**Phenylglycine.**

$$C_6H_5NH.CH_2COOH. \qquad C_3H_9O_2N. \qquad 151.$$

20 gms. of chloroacetic acid are dissolved in 20 c.cs. of water, and 16 gms. of calcium hydroxide added, the whole being kept cool ; a mixture of 20 c.c. of methyl or ethyl alcohol and 60 gms. of aniline is next added, and the whole stirred and warmed until the reaction is complete. The alcohol and aniline are distilled off with steam ; the calcium salt is filtered off and is converted into the sodium salt when cold (see p. 310). The calculated amount of a mineral acid is added to the concentrated solution of the sodium salt, and the phenylglycine thus obtained.




Small crystals. M.P. 126°—127°. (D.R.P., 167698.)

PREPARATION 487.—**Phenylglycine-*o*-carboxylic Acid.**

$$C_6H_4\left\langle\begin{matrix}COOH\\NH.CH_2COOH.\end{matrix}\right. \qquad C_9H_9O_4N. \qquad 195.$$

11·2 gms. caustic potash are dissolved in 100 c.cs. water, and to this are added 9·4 gms. chloroacetic acid and 13·6 gms. anthranilic acid. The solution is warmed on a water bath under a reflux for 2 hours at 60°—80°. Hydrochloric acid is then added to neutralise. The phenylglycine-*o*-carboxylic acid separates out after standing and is filtered off and recrystallised from water. A further yield can be obtained by evaporating the filtrate.

$$C_6H_4\left\langle\begin{matrix}COOH\\NH_2\end{matrix}\right. + ClCH_2COOH \rightarrow C_6H_4\left\langle\begin{matrix}COOH\\NH.CH_2COOH\end{matrix}\right.$$

Colourless crystals. M.P. 200° (with decomposition). Sparingly soluble in water. Solution in alcohol shows a blue fluorescence. (B., 23, 3432.)

PREPARATION 488.—**Glycine** (*Glycocoll, Aminoacetic acid*).

$$CH_2NH_2COOH. \qquad C_2H_5O_2N. \qquad 75.$$

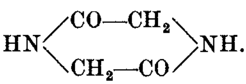
104 gms. of chloroacetic acid are dissolved in an equal weight of water, and this solution slowly run into 1,248 c.cs. of 25% ammonia, the whole being stirred well. When all the acid has been added the solution is set aside for 24 hours and then boiled until no more ammonia is evolved. It is made neutral while hot with a slight excess of copper carbonate, filtered, and the filtrate evaporated until it begins to crystallise. On allowing to cool the copper salt of glycocoll separates as blue needles, is filtered, and washed first with dilute, and then with more concentrated alcohol. The salt is dissolved in water, and the copper precipitated by sulphuretted hydrogen from the boiling solution. The sulphide is filtered off and washed well and the filtrate concentrated to small bulk. On cooling, the glycocoll separates.

$$CH_2ClCOOH + NH_3 \rightarrow CH_2NH_2COOH + HCl.$$

Monoclinic crystals; M.P. 232°—236° with decomposition; soluble in water, almost insoluble in alcohol and ether. (A., 266, 295; O. S., IV., 31.) See also O.S., XIV., 46.

PREPARATION 489.—**Glycocoll Ester and Glycine Anhydride** [*Ethyl ester of amino-ethan acid*] and (2 : 5-*diketopiperazine*).

$NH_2.CH_2.COOC_2H_5$ and



$C_4H_9O_2N$ and $C_4H_6N_2O_2$. 103 and 114.

*Glycocoll Ester.*—50 gms. (1 mol.) glycocoll-ester hydrochloride (see p. 402) are treated with 25 c.cs. of water, which only suffice for partial solution. 100 c.cs. ether are then added, and the whole well cooled in a freezing mixture and treated with 40 c.cs. (excess) of sodium hydroxide (33%). Finally, such an amount of dry, granulated potassium carbonate is added with cooling and shaking as to form a thick paste. After vigorous shaking, the ethereal solution is poured off, the residue is shaken two or three times with ether, and the united extracts, after filtration, are allowed to stand, with frequent shaking, first for 10 minutes with dry potassium carbonate and then for several hours with anhydrous sodium sulphate. The ether is evaporated and the residue is distilled under diminished pressure. At 10 mms. it boils at 51·5°—52·5°, and so the receiver must be well cooled.

$$NH_3Cl.CH_2COOC_2H_5 + NaOH = NH_2.CH_2COOC_2H_5 + NaCl + H_2O.$$

*Yield.*—65% theoretical (25 gms.). B.P. $^{748}$ 148°—149°, with decomposition. (A., 127, 97; J. pr., [2], 37, 166.)

*Glycine Anhydride.*—20 gms. (2 mols.) of glycine-ester are cooled and treated with 12 gms. of water, and the mixture is then allowed to stand

at room temperature for some days. The anhydride separates out during this time in well-defined crystals. It is filtered, washed with a little cold water, and dried under reduced pressure over sulphuric acid.

$$2NH_2CH_2COOC_2H_5 = HN\begin{matrix} \diagup CO—CH_2 \diagdown \\ \diagdown CH_2—CO \diagup \end{matrix}NH + 2C_2H_5OH.$$

*Yield.*—60% theoretical (7 gms.). Colourless plates; turns brown at 245°; melts with blackening at 275°. Sublimes on rapid heating. (J. pr., [2], 37, 173.)

For the direct preparation of glycine-anhydride from glycocoll ester hydrochloride, see B., 39, 2930.

PREPARATION 490.—**Racemic Phenylalanine** [3-*Phenyl*-2-*amino-propan-acid*].

$$C_6H_5.CH_2.CH(NH_2).COOH. \qquad C_9H_{11}O_2N. \qquad 165.$$

50 gms. (1 mol.) of benzylmalonic acid (see p. 135) are dissolved in 250 gms. of dry ether, and 50 gms. ($1\frac{1}{5}$ mols.) bromine are gradually added in daylight. At first the halogen rapidly disappears, and clouds of hydrobromic acid are evolved. At the end the liquid is coloured reddish-brown by the excess of bromine. When it has stood for half an hour the ethereal solution is shaken with a little water, sulphuric acid being gradually added until the red colour of the bromine disappears. The ethereal layer is then separated, again washed with a little water, and carefully evaporated. The solid residue is recrystallised from about 250 c.cs. of hot benzene. Yield, 95% theoretical (65 gms.). The benzyl-bromomalonic acid when dried under reduced pressure at 80° melts at 137° corr.).

The benzylbromomalonic acid containing water is now heated in an oil bath to 125°—130°, and the fused mass evolves carbon dioxide and a certain amount of hydrobromic acid. The reaction is complete in the course of 30—45 minutes. The residue is a yellow oil, which even at a low temperature does not crystallise, and which in the main consists of phenyl-α-bromopropionic acid. For the purpose of purification it is washed with water, taken up in ether, and dried with anhydrous sodium sulphate; the ether is then distilled off. The mobile, almost colourless oil remaining is dissolved in 5 times its volume (excess) of 25% aqueous ammonia, and either heated for 3 hours to 100° in a sealed tube or allowed to stand for 3 to 4 days at ordinary temperature. On evaporation of the ammoniacal solution an almost colourless residue is left, and this chiefly consists of ammonium bromide and phenylalanine. On boiling with absolute alcohol the amino-acid is left undissolved and is recrystallised from hot water.

$$C_6H_5.CH_2CH(COOH)_2 + Br_2 = C_6H_5CH_2CBr(COOH)_2 + HBr.$$
$$C_6H_5CH_2CBr(COOH)_2 \longrightarrow C_6H_5CH_2.CHBrCOOH + CO_2.$$
$$C_6H_5.CH_2CHBr.COOH + 2NH_3 = C_6H_5CH_2.CH(NH_2)COOH + NH_4Br.$$

*Yield.*—55% theoretical (24 gms.). Colourless crystals; soluble in hot water. M.P. 263°—265° with decomposition. (B., 37, 3064.)

PREPARATION 491.—**Diazobenzenesulphonic Acid Anhydride** (*Inner salt of benzenediazonium-hydroxide-4-sulphonic Acid*).

$$[1:4]C_6H_4\left\langle\begin{matrix} N = N \\ SO_3 \end{matrix}\right/ \qquad C_6H_4O_3N_2S. \qquad 184.$$

20 gms. (1 mol.) of sulphanilic acid, previously dried on a water bath and finely powdered, are dissolved, in the heat, in 58 c.cs. (1 mol.) of 2N sodium hydrate; and the solution is diluted until, on cooling to 50°, no crystallisation occurs. This solution is cooled and treated (p. 373) with 10 gms. (more than calculated amount) of sodium nitrite, and the mixture is poured, with constant stirring, into an excess of *cold*, dilute sulphuric acid. In a short time the diazonium compound separates as a white, crystalline mass. To favour crystallisation the liquid is cooled, and after it has stood for some time the substance is filtered off. This compound can be kept in the dry state, but must not be dried at 100°. In dealing with the dry product *care is, however, always necessary, for it sometimes explodes violently when rubbed.*

$$C_6H_4(NH_2)(SO_3H) \longrightarrow C_6H_4(N:NCl)(SO_3H) \longrightarrow C_6H_4\left\langle\begin{matrix} N = N \\ SO_3 \end{matrix}\right/$$

*Yield.*—80% theoretical (16 gms.). Colourless crystals; stable enough to be recrystallised from water at 60°. (A., 190, 76.)

PREPARATION 492.—**Diazomethane.**

$$CH_2N_2. \qquad 42.$$

The apparatus, Fig. 56, is convenient for this preparation, a smaller flask must, however, be used.

75 gms. caustic potash in 180 c.cs. of absolute alcohol are heated, and to the solution are added 15 gms. hydrazine hydrate in 50 c.cs. of absolute alcohol. From a dropping funnel is slowly added, and at such a rate that the reaction does not become too violent, a mixture of 40 gms. chloroform in 50 c.cs. absolute alcohol. At the other end of the condenser there are attached three wash-bottles containing 50, 40 and 30 c.cs. respectively, of absolute ether, and immersed in a good freezing mixture. During the experiment a gentle stream of nitrogen is passed through the apparatus. If the ether in the third wash-bottle is coloured yellow, a fourth wash-bottle is attached. When all the chloroform solution has been added, the diazomethane is removed from flask and condenser by continuing the passage of nitrogen for 10—15 minutes.

The combined ethereal solutions are then placed in a small flask not too tightly stoppered, as diazomethane undergoes continuous decomposition, even in an atmosphere of nitrogen. It should, therefore, be prepared immediately before use, and is usually employed in the form of a solution in ether, alcohol, benzene, or petroleum ether.

$$NH_2.NH_2 + CHCl_3 \longrightarrow N_2CH_2 + 3HCl.$$

Yellow, explosive gas; B.P.—24°. (B., 45, 505.) See also O.S., XV., 3.

The original method of preparing diazomethane is as follows. Methylurethane, formed by the interaction of methylamine and chloroformic ester, is converted into the nitroso compound by the action of nitrous acid, the latter yielding diazomethane on treatment with alcoholic potash.

$$ClCOOC_2H_5 + NH_2CH_3 \longrightarrow CH_3NHCOOC_2H_5$$
$$CH_3NHCOOC_2H_5 + HNO_2 \longrightarrow CH_3N(NO)COOC_2H_5$$
$$CH_3N(NO)COOC_2H_5 + KOH \longrightarrow CH_2N_2 + KHCO_3 + C_2H_5OH.$$

(B., 27, 1888; 28, 855; 35, 897.) For some recent applications as a methylating agent, see J. C. S., 1928, 1310, 1545, 2904; B., 61, [B], 1840; A., 484, 1.

# PART III

## CHAPTER XXXIII

### ORGANIC ANALYSIS

### Detection of Elements present in Carbon Compounds

**Carbon and Hydrogen.**—Some fine copper oxide is heated in a porcelain crucible for a few minutes to drive off all moisture, and afterwards left to cool in a desiccator. A small amount—0·1—0·2 gm.—of the compound is mixed with about 10 times its weight of the dry copper oxide and placed in a dry clean test tube 10—12 cms. long, 4—6 cms. of dry copper oxide are then added, and the tube closed with a cork carrying a delivery tube bent at a right angle. The tube is supported in a horizontal position and gradually heated, beginning first at the unmixed copper oxide and raising it to a high temperature before the compound is appreciably heated. The oxygen of the copper oxide acts as oxidising agent, and if the compound contains hydrogen, water collects on the cooler portions of the tube; if it also contains carbon, the issuing gas, when passed into lime or baryta water, causes turbidity.

**Nitrogen, Halogens, Sulphur and Phosphorus.**—A piece, about 0·5 c.c., of bright sodium or potassium is placed in a small hard glass test tube about 8 cms. long and 1 cm. in diameter. (In testing easily volatile compounds, a longer tube, to act as condenser, should be used.) The end of the tube is gradually heated at some distance above a small flame until the sodium (or potassium) just melts. The tube is withdrawn from the flame, and a small quantity of the compound dropped on to the surface of the molten metal. Generally a brisk reaction, often accompanied by detonations, takes place, and when this subsides the end of the tube is gradually heated to bright redness, at which it is maintained until decomposition is complete, and any excess of sodium is oxidised. By this treatment there is formed: sodium cyanide if nitrogen is present; sodium halide if halogen is present; sodium sulphide if sulphur is present; perhaps, sodium sulphocyanide if both nitrogen and sulphur are present, but when sulphur is present, an excess of sodium should be used in order to prevent the formation of sulphocyanide. While still hot, the tube is plunged into 10 c.cs. of distilled water contained in a small beaker or dish—care should be exercised as the operation is very vigorous; by this the tube is shattered, any alkali metal remaining reacts briskly, a quantity of carbon remains suspended in the liquid, and any cyanide, halide, sulphide or sulphocyanide formed, passes into solution. The

mixture is boiled for a minute, then cooled and filtered through a previously wetted filter paper. The filtrate should be water clear; if not the fusion must be repeated and more care taken to ensure the complete decomposition of the organic compound by longer heating. The filtrate is divided into portions which are tested as follows:—

(*a*) *For Nitrogen.*—To one portion, about 1 c.c. of ferrous sulphate solution and a few drops of ferric chloride solution are added. Hydroxides of iron are precipitated. (If no precipitation occurs, a little caustic soda solution must be added.) The mixture is boiled for 1—2 minutes, and if alkali cyanide—equivalent to nitrogen in the original compound—is present, sodium ferrocyanide is formed. After cooling under the tap, the alkaline mixture is acidified with hydrochloric acid, which dissolves the precipitated ferrous and ferric hydroxides, and the resulting ferric salt reacting on the sodium ferrocyanide forms Prussian Blue. Accordingly a blue or bluish-green precipitate indicates the presence of nitrogen. At times a blue or bluish-green solution is obtained, which only gives a blue precipitate after standing a few hours, or perhaps overnight. (The addition of a little potassium fluoride is often very helpful in bringing down the blue precipitate.) When the test is doubtful, it should be repeated, using more of the alkaline solution, or if the compound contains only a small percentage of nitrogen, it may be necessary to repeat the fusion, using a larger quantity of the compound. Compounds (*e.g.*, diazo-compounds) which evolve nitrogen at moderate temperature generally fail to give a positive reaction by this method, and in such cases nitrogen can be detected by heating the compound with cupric oxide in an atmosphere of carbon dioxide after the manner of a Dumas determination of nitrogen (p. 461), and finding amongst the products a gas which is not absorbed by caustic potash.

For volatile or unstable nitrogen compounds, a mixture consisting of 138 parts of ignited potassium carbonate and 72 parts of magnesium powder may be used in place of sodium (or potassium). Small quantities of this mixture and of the compound are intimately mixed and heated in a glass tube. The mass is extracted with water, filtered, the filtrate made alkaline and tested for cyanide.

Thorpe and Whiteley recommend the following modification of Castellana's method. A mixture of sodium carbonate (1 mol.), potassium carbonate (1 mol.), and magnesium powder (2 atoms) forms a highly active substitute for sodium. A small quantity of the organic compound is intimately mixed with about five times its bulk of this reducing mixture. The crucible containing the mixture is heated, gently at first, then more strongly, until the reaction is over. The residual mixture after cooling is boiled with water and filtered. The filtrate is tested for cyanide as before.

(*b*) *For Halogens.*—If nitrogen has been proved absent by (*a*) a portion of the solution is acidified with nitric acid, and silver nitrate added. A curdy white or yellow precipitate indicates the presence of halogen. If nitrogen is present, the solution, after acidification with nitric acid, must

be boiled until all hydrocyanic acid is expelled before silver nitrate is added.

Halogens may also be detected by Beilstein's test—a piece of pure copper oxide, held by means of a platinum wire around it, is heated in a Bunsen flame until it ceases to colour the flame green. It is then allowed to cool, and a little of the compound is placed on it. If, on heating again, there appears a bright green flame accompanied by a blue zone round the oxide (due to the volatilisation of copper halide), the presence of a halogen is indicated.

Certain nitrogenous compounds, however, give a volatile cuprous cyanide in this test which produces a green flame coloration. The presence of halogen must therefore be confirmed by other tests.

A third test for the presence of halogens consists in heating the compound along with an excess of pure lime in a glass tube. The mass is afterwards extracted with water, and tested with silver nitrate.

(*c*) *For Sulphur.*—To a portion of the alkaline filtrate a few drops of a freshly prepared solution of sodium nitroprusside are added. A violet or purple coloration indicates the presence of sulphur.

Other methods—in all of which the resultant sulphate is precipitated with barium chloride—for the detection of sulphur in compounds, are: (*a*) oxidation with sodium peroxide (see p. 472); (*b*) oxidation with sodium carbonate and potassium nitrate; (*c*) oxidation with fuming nitric acid in sealed tubes.

(*d*) *For Phosphorus.*—About 1 c.c. of the alkaline filtrate is heated with 3 c.cs. of conc. nitric acid for a few minutes. To this solution after cooling, ammonium molybdate solution is added, and the whole warmed. A crystalline yellow precipitate of ammonium phosphomolybdate on standing indicates the presence of phosphorus.

Other methods for the detection of phosphorus involve oxidation to phosphoric acid by means of (*a*) sodium peroxide; (*b*) sodium carbonate and potassium nitrate; (*c*) fuming nitric acid in sealed tubes.

The presence of phosphorus may also be ascertained by heating the compound with magnesium powder, and moistening the cold product with water, whereby phosphine (recognised by its smell) is liberated from the magnesium phosphide.

**Metallic Radicles.**—The organic matter in the compound is destroyed either (*a*) by heating to redness for some time in contact with air in a quartz or porcelain crucible, or (*b*) by oxidising with a mixture of conc. nitric and sulphuric acids. After decomposition is complete, the residue is examined by the usual tests for inorganic radicles. In (*a*) volatile radicles such as mercury, arsenic and ammonium will be lost.

# CHAPTER XXXIV

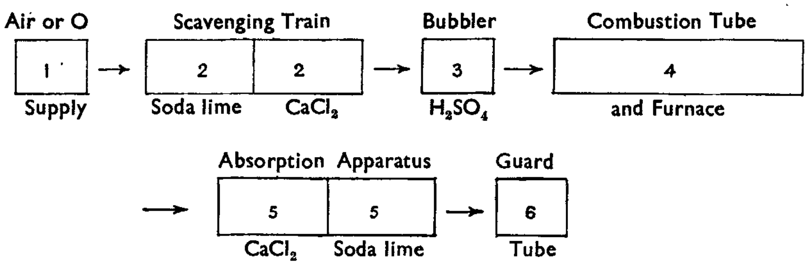
## ESTIMATION OF CARBON AND HYDROGEN

### (A) Macro Method

THE principle involved in combustion is the complete oxidation of **C** and **H** in the compound to $CO_2$ and $H_2O$ by means of air or **O**. By the separate absorption of these two substances the percentages of **C** and **H** can be calculated. For many years the macro method in general use has been that originally due to Liebig, in which 0·15—0·25 gm. of substance is required for the analysis.

The apparatus gives good results, but is cumbersome and uncomfortable in its operation. Within the last 20 years there has been an increasing tendency towards the evolution of finer and more convenient methods. These, although not yet in general use, will be considered later.

The sequence of operations is outlined in the following diagram :—




*The air or* **O** *supply* [1] generally comes from tanks under slight pressure. Acidic impurities and water vapour are removed in [2].

*The scavenging train* [2] (soda lime and anhydrous $CaCl_2$) can be con-

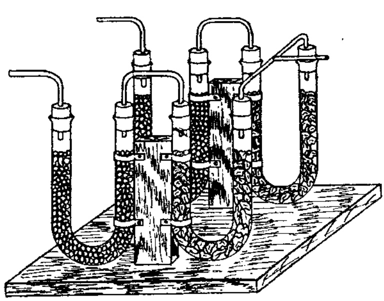


FIG. 58.

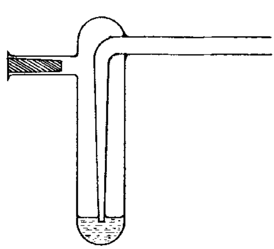


FIG. 59.

tained in large U-tubes (Fig. 58) linked by glass tube connections passing through rubber stoppers inserted in the ends of the U-tubes. The rubber

stoppers may be coated with wax or shellac to make them gas-tight. Soda lime and $CaCl_2$ are nowadays obtainable in granular form (12—20 mesh), from which any fine powder can be removed by sieving.

*The glass bubbler* [3] (Fig. 59) contains a small amount of conc. $H_2SO_4$, through which the air or **O** is passed. By uniform control of the bubble rate, regular combustion of the material can be ensured.

*The combustion tube* [4] should be of difficultly fusible glass, 12—18 mms. internal bore, 15—21 mms. external bore, and 75—80 cms. in length. The nature of the filling put into this tube depends on the elements in the substance to be analysed.

(*a*) **Substances containing only C and H or C, H and O.**—A loose plug or spiral of oxidised **Cu** gauze, 1—2 cms. long, is placed in the tube 5 cms. from one end (Fig. 60); wire-form **CuO** is poured in from the other end until there is a layer about 45 cms. long. A second plug of oxidised **Cu** gauze is introduced to keep this **CuO** in position. A spiral of oxidised **Cu** gauze (15 cms. long) is prepared by tightly rolling **Cu** gauze (40 mesh) round a stout **Cu** wire until the roll neatly fits the tube. The projecting ends of the wire are bent into loops close to the gauze, and the spiral oxidised by heating in a blowpipe flame. The spiral, when cold, is pushed into the

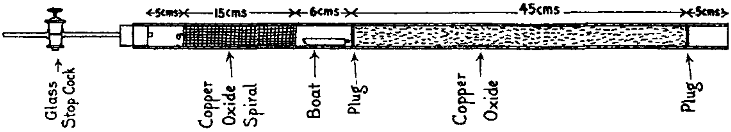



FIG. 60.

tube to a distance of 5 cms. from one end, the loops enabling it to be moved backwards and forwards in the tube by means of a stout hooked **Cu** wire. The combustion tube is fitted with two good red indiarubber one-holed stoppers. The stopper next the oxidised **Cu** spiral carries a glass delivery tube; the latter is provided with a ground-glass stopcock and serves as an inlet for the purified air or **O**.

(*b*) **Substances containing C, H, O and N.**—Under ordinary conditions of combustion, substances containing **N** yield fair quantities of oxides of **N**. As these would be absorbed in the soda lime tube and cause increase in the apparent **C** content, steps are taken to decompose them. This is done by passing the combustion vapours over pure reduced **Cu**, when the oxides of **N** are decomposed, giving **N**, which passes through the absorption train. The **CuO** filling (45 cms.) used in the above tube is reduced to 35 cms. and is placed in the tube so that it commences about 15 cms. from the exit end of the combustion tube. A **Cu** gauze spiral (10 cms. long) is prepared as in (*a*), and is heated to redness in a blowpipe flame, care being taken to avoid fusing or burning the **Cu** gauze. The spiral, while hot, is dropped into a boiling tube with a wad of asbestos or glass wool, soaked with methyl alcohol, at the bottom.

The alcohol reduces the oxidised gauze and is converted at the same time to formaldehyde. The spiral, when cool, is removed, placed in a

clean boiling tube, and heated in an oven at 100°—120° for a short time. It should then be kept *in vacuo* over $\mathbf{CaCl_2}$.

(*c*) **Substances containing also S or Halogen.**—For the combustion of these substances the **CuO** filling is replaced by a mixture of **CuO** and $\mathbf{PbCrO_4}$ granules. The $\mathbf{PbCrO_4}$ retains the **S** and halogen as sulphate and halide, and thus prevents them reaching the absorption train. The following precaution must be taken: the mixture must not be heated so strongly as before, otherwise it fuses to the glass, causing ultimate splintering of the combustion tube; and further, $\mathbf{PbSO_4}$ is slightly unstable

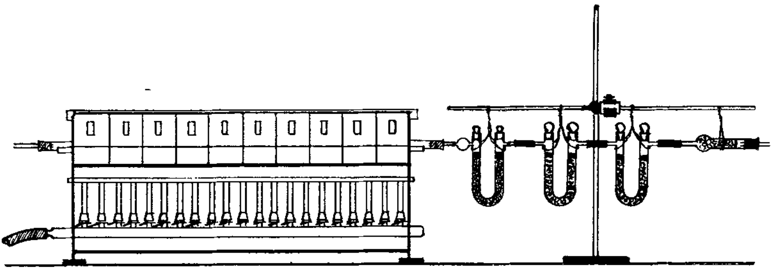


FIG. 61.

and lead halide slightly volatile at higher temperatures. The combustion of halogen-containing substances may be carried out by means of **CuO** alone if a **Ag** spiral is inserted at the exit end of the combustion tube to retain the halogen.

In the micro method of combustion, substances containing any of these elements (**N, S** and halogen) can be combusted in one tube by the use of the so-called "Universal Filling" (see section on Micro-analysis, p. 453).

**Furnaces.**—Gas- or electrically-heated furnaces (Fig. 61 or 62) can be used. The gas furnace consists of a series of Bunsen flames impinging

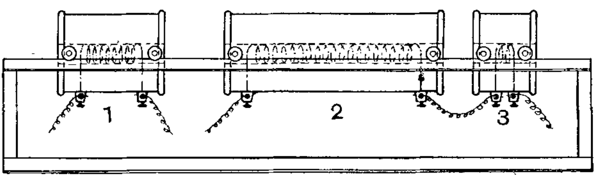



FIG. 62.

on an iron bed or trough lined with thin sheet asbestos, the burners being so arranged that they can be controlled separately. The combustion tube is carried in the bed or trough, and around and above it on either side are series of fireclay tiles arranged to act as muffles. These can be removed at will to regulate the temperature of the combustion tube and rate of combustion.

**Electrically-heated Furnace.**—The furnace (Fig. 62) is very simple to manipulate and free from the objections of the ordinary gas furnace; it may be operated on the laboratory bench. It consists of three separate heating units (1, 2 and 3). Units 2 and 3 are used to heat the oxidising

filling, while the movable unit 1 heats the portion of the tube in proximity to the boat. The heating elements consist of suitable windings of special resistance wire embedded in a cylindrical matrix around the combustion tube.

The heating units are movable on the supporting structure, the tube support running centrally through the units. The furnace is explored at the outset, using a thermocouple to determine the temperature at regular intervals inside the furnace. Suitable resistances are chosen to give a temperature of about 800° in units 1 and 2. The resistance of unit 3 is chosen so that the temperature may be varied between 600° and 800°, depending on the elements present in the compound. In the combustion, units 2 and 3 are stationary, while 1, after having been raised to a temperature of 800° over the **CuO** spiral, is brought gradually nearer to the substance in the combustion tube, ultimately enclosing it completely.

A glass combustion tube, longer than that used in the ordinary furnace, is desirable, viz., 120 cms.

*The absorption train* [5].—The usual agent for the absorption of $H_2O$ is

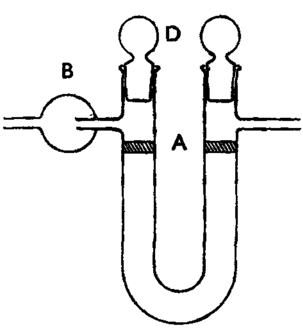



FIG. 63.

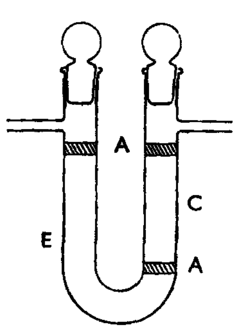



FIG. 64.

$CaCl_2$ in granular form (12—20 mesh), although $Al_2O_3$ or conc. $H_2SO_4$ adsorbed on small pumice granules can also be used. The $CaCl_2$ granules are most conveniently carried in a U-tube fitted with ground-glass stoppers (Fig. 63). These stoppers are pressed into position after smearing with vaseline or some compound such as Steven's cement.

As commercial $CaCl_2$ contains small amounts of $CaO$, it is often advisable to pass a current of $CO_2$ through the tube for a minute or two. The excess $CO_2$ is then removed in a gentle current of air.

Soda lime E is usually employed for the absorption of $CO_2$, an indicator being sometimes added to show when it is exhausted. The soda lime is carried in tubes (Fig. 64) similar to Fig. 63, except that no glass bulb, B, is required. Two soda lime tubes (in series) are used in every combustion. If the combustion has been properly carried out there ought to be no increase in weight of the second tube. Since $H_2O$ vapour may be evolved in the absorption of the $CO_2$ by the soda lime, a small trap of $CaCl_2$ is inserted (C) in the exit limb of each tube to prevent loss of this $H_2O$. Glass wool plugs A retain the absorbents in position.

In filling the **$CaCl_2$** and soda lime tubes, care should be taken that dust from these substances does not fall into the entry or exit tubes. Before inserting the ground-glass stoppers D, the ground-glass portion of the tube should be thoroughly cleaned with a cloth. All excess of vaseline should be carefully removed from the external parts of the stoppers D after insertion. If these points are not observed, irregularity in weight of the tubes may be found. A **$CaCl_2$** tube will serve for at least 2 *dozen* combustions, but the contents of the soda lime tubes should be renewed after every 4 combustions. These absorption tubes are supported in the balance by aluminium wire links, whose looped ends slip over the entry and exit tubes. Absorption tubes are connected together with short pieces of rubber tubing. This tubing should be fresh and of best quality and replaced by new tubing at regular intervals. A type of tubing with a fairly stout wall (not pressure tubing) is available. When connecting two absorption tubes the rubber should be worked over the tube ends until they meet inside the rubber tubing.

An alternative form of apparatus for the absorption of **$CO_2$** is the **KOH** bulb, which is more complicated; one type is shown in Fig. 65. The bulbs are filled with a solution of **KOH** containing 50 gms. in 50 c.cs. of water. **NaOH** is not used owing to the tendency for **$NaHCO_3$** to separate in the apparatus. The removable side tube is filled with granular **$CaCl_2$** and has a loose plug of cotton-wool at each end. In order to fill the bulbs with **KOH** solution the side tube is removed and a length of rubber tubing attached in its stead; the other end of the apparatus is dipped into a basin containing the **KOH** solution and suction is applied until a quantity of liquid, almost sufficient to fill the bulbs, is transferred. After filling the bulbs, that part of the apparatus immersed in the **KOH** solution is dried with pieces of rolled filter paper; the ground-glass joint of the **$CaCl_2$** tube is smeared with vaseline and the side tube replaced. Stoppers of rubber pressure tubing and glass rod are attached and these are only removed when the apparatus is in use. When in use, the arm-tube is joined by pressure tubing to a guard tube [6] containing **$CaCl_2$** and soda lime. The other end of the **KOH** apparatus is similarly joined to the **$H_2O$** absorption tube. The **KOH** solution should be renewed after every two combustions.

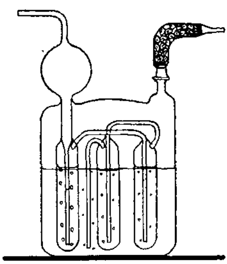


FIG. 65.

## Preliminaries to the Process of Combustion

After erecting and charging the apparatus, it is advisable first to determine that it is gas-tight. This is done by setting the air tank in operation and opening all stopcocks so that there is a free passage for gas through the apparatus. If the last stopcock on the terminal soda lime tube is then closed, air should cease to pass through the bubbler after a short interval. If the bubbler continues to function, then the stopcocks

on the soda lime and $CaCl_2$ tubes should be successively closed (moving towards the furnace). Cessation of bubbling at any point in this procedure will indicate which of the stopcocks or rubber connections in the absorption train are defective. If leakage continues, then the rubber stoppers in the combustion tube and the connecting parts between the bubbler and combustion tube should be checked. If the air and **O** tanks exhaust themselves too rapidly, it may be a sign of leakage in the scavenging train. This should be carefully noted, as air which has not been fully purified may enter into the combustion tube.

If everything is in order, the next step is the burning-out of the combustion tube. This is done by disconnecting the absorption train and starting the air flow. Small flames should be slowly and regularly lit along the combustion tube, care being taken to avoid rapid and uneven heating at first; otherwise the combustion tube may crack during its first heating. The temperature should be slowly and steadily raised, and during the process water will be seen to come from the filling. This can be removed by inserting a rolled filter paper into the exit end of the combustion tube at intervals, or by holding a hot furnace tile near that portion of the tube. To ensure complete removal of $H_2O$ and any carbonaceous impurity from the tube, it should be heated for a few hours, preferably with the passage of **O**. At the end of the first heating the tube should be slowly cooled.

**Blank Experiment.**—The proper functioning of the apparatus can be controlled by carrying out a blank experiment in which every operation of a combustion proper is performed in absence of the substance. Air is passed through the tube while only the **CuO** portion is heated. In the meantime the absorption tubes are wiped and weighed ($CaCl_2$ tube first). After each tube is weighed, the rubber caps are replaced. When the weighings are completed the combustion train should be attached to the tube. The bulb end of the $CaCl_2$ tube is attached to the combustion tube, and the soda lime tubes attached to the $CaCl_2$ tube so that the $CaCl_2$ traps are away from the furnace. The guard tube is then affixed to the last soda lime tube. The flow of air or **O** is then temporarily stopped and the rubber stopper at the entry end of the combustion tube detached. The removable **CuO** gauze spiral is then withdrawn with a clean, hooked, stout **Cu** wire and laid on a clean furnace tile. An empty porcelain or quartz boat, which has previously been burnt out in a blowpipe flame until constant in weight, is then pushed into the tube with the **Cu** wire until it is within half an inch of the hot **CuO**. The oxidised **Cu** gauze spiral is then replaced, the tube closed again, and the passage of air recommenced. Burners are now lit underneath the spiral and boat. After 15 minutes, **O** can be turned on and passed for 15 minutes, and then air for 20 minutes (total 50 minutes).

The absorption train can then be detached, removed to the balance room, wiped carefully with a clean hairless cloth and kept 15—20 minutes to attain constant temperature. The tubes are then weighed without their rubber caps. If the apparatus is in proper working order, and the

manipulation efficient, only very small increases in the weights of the absorption tubes (0·0003 gm. at most) should be apparent.

**The Combustion.**—The manipulation is much the same as for the blank experiment, the part of the tube containing the oxidising filling being heated while substance and tubes are being weighed. The boat is first weighed and then 0·15—0·2 gm. of substance placed in it and accurately weighed; the absorption tubes are then cleaned and weighed. The latter are attached and the boat inserted as before.

In general, liquid substances of B.P. above 170° may be weighed directly into the boat. If the substance is hygroscopic the boat must be enclosed and weighed in a dry stoppered tube. Volatile liquids must be weighed in a small sealed glass bulb (Fig. 66) which is placed in the boat after filing and breaking off the neck of the bulb.

FIG. 66.

Two or three burners under the **CuO** spiral, but not within 5 cms. of the boat, are now lit. The flames from the burners are gradually increased in size until the tube above them attains a dull red heat when the corresponding tiles are in position. Next follows that part of the operation, the successful carrying out of which is essential in order to obtain accurate results, namely, the gradual combustion of the substance. The bubbler must be carefully watched at this stage; if the rate of bubbling slackens markedly, heating near the boat should be cut down and tiles removed. Further heating should be done very slowly, as any sudden rush of vapour, which might lead to imperfect combustion, is to be avoided. The remaining burners, beginning with those farthest from the substance, are lit and gradually turned on. The first indication of combustion is the appearance of moisture on the exit end of the tube. With easily volatile substances the boat is heated at the outset by means of hot tiles brought from an already heated part of the furnace. As the combustion proceeds, the heat near and around the boat is increased until all the substance disappears. When the combustion is nearly finished the stream of air is shut off and a stream of **O** immediately turned on. **C** may persist in the boat, but the passage of **O** for a short time usually removes this, unless in exceptional cases. Finally the whole tube is heated strongly while air is passed for 15 minutes. The absorption tubes are then detached, wiped, cooled and weighed as described for the blank experiment.

The weights of $\mathbf{CO_2}$ and $\mathbf{H_2O}$ produced in the combustion enable the percentage of **C** and **H** to be calculated as follows :—

$$\%\ \mathbf{C} = \frac{\text{wt. of } \mathbf{CO_2}}{\text{wt. of substance}} \times 27{\cdot}27.$$

$$\%\ \mathbf{H} = \frac{\text{wt. of } \mathbf{H_2O}}{\text{wt. of substance}} \times 11{\cdot}19.$$

The results for each element should not differ by more than 0·3 from the theoretical.

## (B) Micro Method

The macro method of combustion held the field for many years, and it is interesting that when a change came it should be towards the other extreme. The entry of Pregl with his micro-combustion method in 1912 into this sphere marked the first major change in combustion technique for a long period. This extreme change had perhaps been forced by the rapid development of biochemistry and of other types of research in which very small quantities of material had to be handled, and amounts of 0·2—0·25 gm. were not always available for analysis. The use of 2—3 mgs. of substance for a combustion, and correspondingly small amounts of substance for other analyses, has only been rendered possible by the development of the micro-balance (reading to 0·000001 gm.). A full description of the construction and manipulation of this balance and the methods of Pregl are to be found in his " Quantitative Organic Micro-Analysis " (translations by Fyleman or Daw).

Whilst the fundamental principles of combustion are common to both macro and micro methods, the actual conditions and mode of operation are markedly different. In the micro method the importance of absolute cleanliness and neatness of operation cannot be overstressed.

**Estimation of C and H.**—The open-ended tube of the macro method is replaced by a tube drawn out to a narrow snout at one end. The other

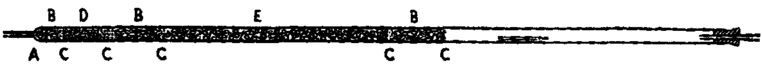



Fig. 67.

end of the tube carries a rubber stopper having a tapered delivery tube for the air or **O** supply. Alternatively, the wide end of the combustion tube can be closed with a solid rubber stopper and the air or **O** led in through a glass tube sealed on at right angles to the combustion tube a few cms. from the end. The snout should be of approximately the same diameter as the entry tube of the absorption train. In the snout end of the tube is placed a packing plug of Gooch asbestos which is compressed to ensure that the combustion gases emerge from the tube at uniform rate. The customary filling of **CuO** is used if only **C, H** and **O** are present, but Pregl made considerable advance in the adoption of the " Universal Filling " which enables **C** and **H** to be estimated in the presence of **N, S,** or halogens. Such a filling is illustrated in Fig. 67. A is the asbestos packing plug; BBB, **Ag** wool plugs; CCCCC, asbestos retaining plugs; D, granular $PbO_2$ (or asbestos impregnated with $PbO_2$); E, $CuO$ + $PbCrO_4$.

The **Ag** wool plugs serve to remove halogens, the $PbO_2$ to decompose oxides of **N** into **N,** the $PbCrO_4$ to retain **S.** Some workers (Linder, Ber., 1932, 65, 1696) object to the use of $PbO_2$, and employ a layer of reduced **Cu** at the snout end of the tube as in the macro method. If $PbO_2$ is used, the portion of the tube containing this part of the filling must be kept at constant temperature, since the amount of moisture

retained by this substance varies markedly with temperature. This is done by surrounding the tube with a heating mortar or jacket containing boiling *p*-cymene or dekalin.

Usually the air and **O** are supplied from tanks. Cylinders may be used, but in that case a suitable gauge for controlling pressure must be intro-

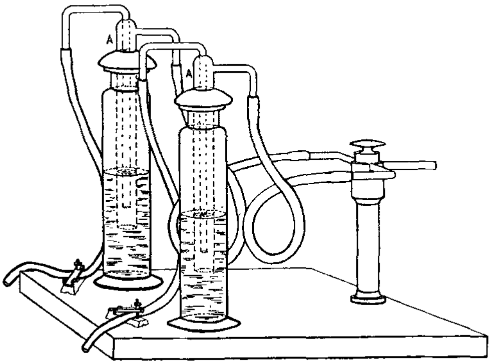



FIG. 68.

duced. If tanks are used, then the air or **O** passes first into the pressure regulator (Fig. 68).

The glass sleeve A can be raised or lowered in the conc. $\mathbf{H_2SO_4}$ and the pressure in the combustion tube altered thereby. With a head of 5—7 cms. of $\mathbf{H_2SO_4}$, and proper adjustment of the packing plug in the combustion tube, air ought to pass through the apparatus at the rate of 3—4 c.cs. per

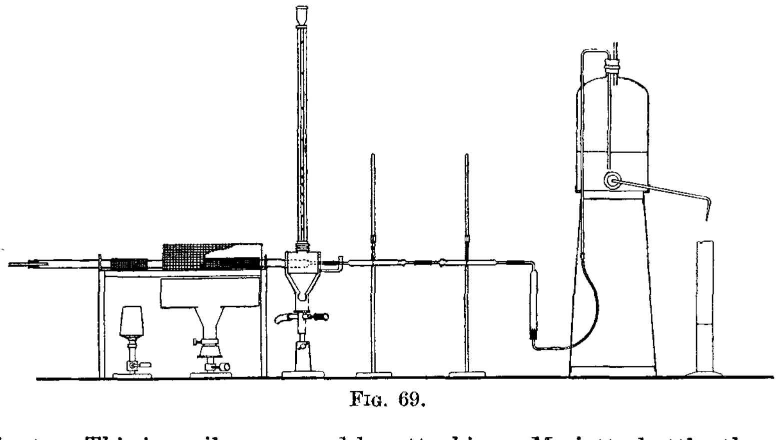


FIG. 69.

minute. This is easily measured by attaching a Mariotte bottle, the use and construction of which are described by Pregl (*loc. cit.*), to the exit end of the absorption train (Fig. 69).

From the regulator the air passes through the bubble-counter and cavenging tube (Fig. 70) which are often made in one piece. Strong **KOH** solution is used in the bubble-counter. Next in the scavenging tube

comes soda lime, and then $CaCl_2$ or $Mg(ClO_4)_2$. The same drying agent is used as in the absorption tubes. The air or **O** passes from the scavenging apparatus into the combustion tube.

The tubes used for the absorption of the $H_2O$ and $CO_2$ formed in the combustion are of a very different type to those used in the macro method. Many workers use a straight tube (Fig. 71 (*a*)). Some use tubes of the Bobranski and Sucharda pattern (*b*). The simplest tube is the modifica-

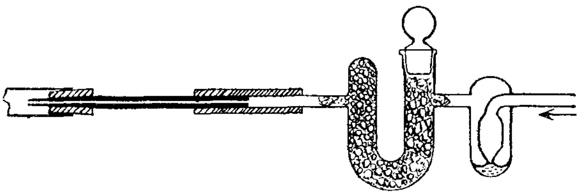


FIG. 70.

tion of Roger and McKay (J. S. C. I., 1935, 54, 46T) (*c*). The same type of tube can be used for both absorbents. $H_2O$ is absorbed in $CaCl_2$ or $Mg(ClO_4)_2$. $CO_2$ is absorbed by soda lime (often with an indicator added), and recently asbestos impregnated with **NaOH** has been introduced and found satisfactory. In the $CO_2$ absorption tube a small amount of $CaCl_2$ or $Mg(ClO_4)_2$ is placed in the exit end to prevent loss of $H_2O$ from the tube. These tubes are closed when not in use by small caps of rubber tube and glass rod. For rapidity in weighing, and to minimise sources of error, the tubes should be counterpoised approximately by small glass flasks

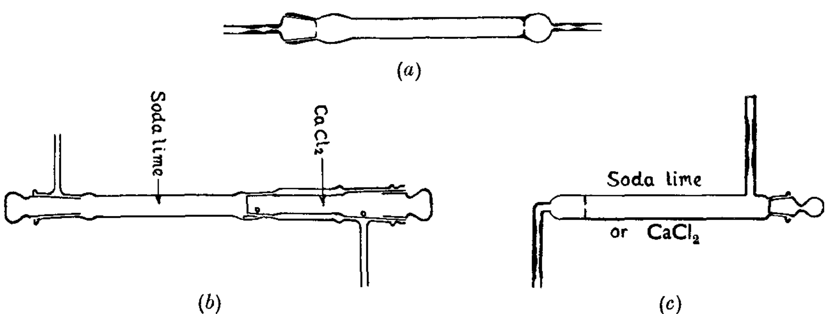



FIG. 71.

containing fine lead shot. These counterpoises should be kept in the balance case or enclosure.

**The Combustion Proper.**—The burners are lit under the heating mortar and oxidising portion of the combustion tube while air is passed. In the meantime the caps are taken off the absorption tubes, which are then carefully wiped with chamois leather. Care should be taken that no part of the tubes is wiped in both directions, otherwise they may become electrified and give trouble in weighing. If there is any doubt whether electrification has occurred the tubes can be discharged by bringing into

contact with a water pipe. The tubes are placed on a suitable stand to attain equilibrium while the boat is weighed (a suitable counterpoise for the boat can be made of stout platinum or aluminium wire); 2—3 mgs. of the substance are placed in the boat and the weighing completed.

The water absorption tube is then placed on the left-hand balance-pan hooks and its counterpoise on the other pan. It can be weighed in a minute or two, taken out, the caps replaced and the $CO_2$ absorption tube weighed in a similar manner. The $H_2O$ absorption tube is then connected to the combustion tube snout, and for this purpose pressure tubing which has been impregnated with wax makes the most satisfactory joint. The soda lime tube is then joined to the $H_2O$ absorption tube so that the soda lime is nearest the furnace. A small guard tube containing $CaCl_2$ or $Mg(ClO_4)_2$ and soda lime is attached to the $CO_2$ tube. Finally, if a Mariotte bottle is used, this is connected to the guard tube. The Mariotte bottle should be adjusted so that it exercises only a very slight suction effect. The boat is then pushed into the combustion tube with a length of stout platinum wire and left at a short distance behind the filling. The tube is then closed and air passed. A small Bunsen is lit some distance behind the boat and the heat conducted over the latter by means of a wire gauze cover which can be moved towards it. By this means the substance can be distilled slowly and regularly from the boat into the filling. The bubble-counter should be carefully observed. If the combustion is being carried out too quickly, the bubble rate will slow down markedly, in which case the rate of heating of the substance should be reduced. As the combustion proceeds, $H_2O$ collects at the snout end of the combustion tube, and can be driven into the glass bell of the $H_2O$ absorption tube by means of a hot metal rod or small strip of wire gauze. **O** should be passed for about 10 minutes during the middle stage of the combustion, which should occupy roughly 30 minutes. The tubes are then detached and, without replacing the caps, wiped carefully, and kept for 15 minutes before weighing.

*Notes.*—The micro balance, reading as it does to 0·000001 gm., is a delicate instrument. It should be kept on a strong, steady support in a part of the room as free from draughts, heat currents, etc., as possible. It is often better to enclose it in an external housing, where it can be kept clean and away from fumes. All weighings should be carried out whenever possible by means of counterpoises. The absorption tubes should be carried on stout wire stands, and the complete filling of the soda lime tube renewed every few combustions. The combustion should be carried out as smoothly and regularly as possible.

The apparatus and the results can always be checked by carrying out a blank combustion in which all manipulations are repeated, but with no substance in the boat.

### (C) Hemi-Macro Methods

Whilst the ultimate ideal in organic analysis is the general adoption of micro methods, it has to be appreciated that such ideals cannot always

be realised. The micro methods require a high degree of technical skill and the apparatus and balance are expensive and delicate. Within recent years, therefore, there has been a definite tendency to employ hemi-macro methods in which the ordinary analytical balance (reading to 0·0001 gm.) can be utilised. Hemi-macro balances are on the market, but a well-kept analytical balance (preferably air-damped or chainomatic) is quite adequate. (Good and reliable methods are now available wherein 20—50 mgs. of substance are combusted.) In such methods, counterpoises should be used whenever possible, as this tends to eliminate error in weighing. The chainomatic and some air-damped balances are of particular value on this account, since, by the aid of counterpoises, no weights require to be used during the analysis. Care and cleanliness are predominant factors in hemi-macro manipulation, and for this reason alone the method serves as an excellent introduction to micro technique. Space is not available for descriptions of all the methods in use. Bobranski and Sucharda, in their book "Semi-micro Methods for the Elementary Analysis of Organic Compounds" (translated by Ferguson), give full descriptions of their methods for certain of the estimations required in organic chemistry. Their apparatus for the determination of **C** and **H** in organic compounds is an enlarged edition of the Pregl apparatus, and the manipulation is much the same. It has one definite advantage in the addition of an automatic regulator, whereby the size of the flame under the boat is controlled by the pressure inside the combustion tube. This obviates the risk of distilling the substance too quickly from the boat and causing a blow-back. It also minimises the amount of attention required during the combustion.

A simple method for the determination of **C** and **H** is that of Roger and McKay (*loc. cit.*). Amounts of substance from 20—40 mgs. are used and the heating mortar of the Pregl method is dispensed with and simple fillings of the macro type are used in the combustion tube.

## General Description of Method

The combustion tube, 60 cms. long and 1·4 cms. internal diameter, made of stout Pyrex or Monax combustion tubing, is drawn to a snout at one end, the drawn-out end being 5 cms. long and 0·4 cm. diameter (see Fig. 72). In the snout end is placed a packing plug of Gooch asbestos, timed to allow a rate of flow of air of about 16 c.cs. per minute when the tube is packed and hot. This timing is done with a Mariotte flask (Fig. 69) as described by Pregl, with a pressure of 5—7 cms. in the pressure regulator (see description of scavenging train). Various fillings can be put in the tube as conditions require.

**The Scavenging Train.**—Air or **O** is taken from the tank and is first led through a $H_2SO_4$ pressure regulator of the Pregl type. The glass tubes of the regulator should be made of greater diameter than those of the true Pregl regulator. The air passes from the regulator through a bubbler (Fig. 59) containing $H_2SO_4$, and then successively through U-tubes containing soda lime and $CaCl_2$ (the absorption tubes of the old macro

method (p. 449) can be used for this purpose). On the exit limb of the **$CaCl_2$** tube a rubber stopper is placed which fits directly into the end of the combustion tube.

**The Absorption Train.**—The body of the tube (Fig. 72) is straight and closed at one end by a ground-glass stopper. Immediately below the stopper an entry (or exit) tube with constrictions is joined at right angles to the body. At the other end of the body is a glass plate with a hole in it emerging into a glass bell. The tip of the bell finishes in a small diameter tube (with constrictions) at right angles to the main body. These tubes possess the advantage of being easily handled and form a very compact absorption train. Moreover, once they are filled, the glass stopper need not be touched. They can also be adapted for micro combustions by altering the dimensions.

In filling the tubes a small wad of glass wool is first placed over the perforated glass plate. In the case of the soda lime tube, a layer (1—1·5 cms.) of **$CaCl_2$** is then placed on this wad and is held in place by another small wad of glass wool. The rest of the tube is filled with soda lime capped with a small glass wool wad. The stoppers must be carefully

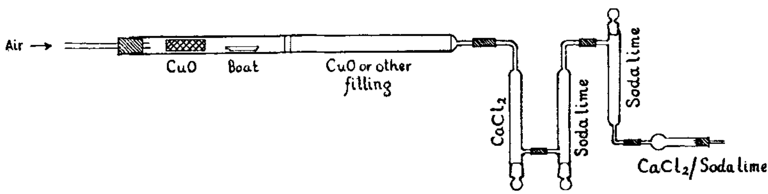



FIG. 72.

greased, and any grease which may emerge over the top when they are pushed home must be completely removed before weighing.

The **$CaCl_2$** tube is attached with a piece of pressure tubing to the snout end of the combustion tube through the tube entering the glass bell. The first soda lime tube is attached to the **$CaCl_2$** tube through the small tube entering under the stopper. The second soda lime tube is attached to the exit tube of the first in a similar manner. The absorption train is protected with a small tube containing **$CaCl_2$** and soda lime.

**Weighing.**—The weights, if used, must be accurately calibrated. For example, the two 0·2 gm. + the 0·1 gm. weights should give the same swing of the balance pointer to within a fraction of a division against the 0·5 gm. The greatest discrepancies are often found in 1 gm. weights. The ideal system is to use small glass counterpoise flasks adjusted with small lead shot to slightly under the weights of the respective absorption tubes and do all weighings preferably on a chainomatic (or air-damped) balance. With this combination the use of any weights is avoided, and a very common source of error in the method disappears. The counterpoises should be kept in an empty desiccator along with the aluminium loop used for suspending the tubes in the balance.

The first stage in the weighing operations is the wiping of the absorp-

tion tubes with chamois or clean hairless cloth. The wiping should be done in one direction only, as for micro tubes. The tubes are placed on wire supports in a box and allowed to settle while the substance is weighed into the boat. Very good quartz boats are now available which keep remarkably constant in weight over long series of combustions. The tubes are then weighed, being carried in the balance by suspension from the beam hook with a clean aluminium loop, the loop being transferred from tube to tube as required. As each tube is weighed it is closed with small rubber and glass rod caps. After the combustion the tubes are brought back to the balance room, wiped, and left uncapped for 15 minutes. By that time they are usually constant in weight.

The method can be easily checked by carrying out a blank combustion. This serves a two-fold purpose. In inserting the boat and attaching the absorption tubes it is impossible to avoid the entry of a small amount of $\mathbf{CO_2}$ and $\mathbf{H_2O}$, and the extent of the experimental error can thereby be gauged. This is particularly noticeable when a substance is difficult to combust and requires a long burning period. The increase in weight of the tube from an ordinary blank combustion seldom exceeds 0·0003 gm. per tube. Further, if the apparatus is not in proper working order, or if the weights are not consistent, the effect will be apparent in the blank.

### Determination of C and H in absence of N, S or Halogen

This is done in a snout-ended tube (see Fig. 67) with an asbestos plug packed in the snout and timed to allow a rate of flow of air of about 15 c.cs. per minute. A filling of about 24 cms. of wire-form **CuO** is used, and this is held in place by a small asbestos plug. Behind the boat is placed a short **CuO** gauze spiral.

The combustion train is first attached to the combustion tube by reliable rubber connections and the boat then placed in position. The **CuO** spiral behind the boat is heated and the substance *slowly* distilled into the previously heated **CuO** filling. A short time after the commencement of the combustion $\mathbf{H_2O}$ will make its appearance in the snout end of the tube. It should be driven into the $\mathbf{CaCl_2}$ tube by holding a pair of hot tongs around the tube. This should be done regularly. After 10 minutes, **O** is switched on and passed for 15 minutes, or until the contents of the combustion tube are completely oxidised. Air is passed again for about 15 minutes to displace the **O**. The absorption tubes are detached and treated as already described.

### Determination of C and H in presence of N

An asbestos packing plug (rate 14 c.cs. per minute) is placed in the snout of the tube. Then comes a filling of wire-form **CuO** (or a mixture of **CuO** and $\mathbf{PbCrO_4}$ for substances containing both **N** and **S**), held in position by a short **Cu** gauze plug (total length 10 cms.). Next to this is placed a removable, reduced **Cu** gauze spiral (8 cms.), followed by a removable

oxidised **Cu** gauze spiral. Behind the boat a short oxidised **Cu** spiral is placed.

The absorption tubes are first attached. Then the reduced spiral is placed in position, followed by the oxidised spiral. Next to that comes the boat and then the short oxidised spiral. The portion of the tube containing the removable oxidised **Cu** spiral is heated (the permanent filling having been heated during the weighing operation), and a gentle heat is applied to the portion containing the reduced spiral. A slow current of air should be used at first, which is controlled by adjusting the stopper of the scavenging $\mathbf{CaCl_2}$ tube and watching the bubbler. As the substance distils and decomposes in the **CuO** spiral the rate of air supply should be increased until normal. After 15—20 minutes **O** is turned on for 10 minutes, followed by air for 20 minutes.

### Determination of C and H in presence of Halogen or S

Behind the packing plug in a snout-ended tube, a **Ag** gauze spiral (5 cms.) is placed and held in position by a layer of asbestos (0·5 cm.). A filling of a mixture of wire-form **CuO** and $\mathbf{PbCrO_4}$ is inserted and held in place by an asbestos plug (0·5 cm.). Between the boat and this last plug is another **Ag** spiral (5 cms.). The combustion is carried out in much the same manner as described for **C—H** compounds.

See also J. S. C. I., 1935, 46; Am. Soc., 1917, 2055; J. C. S., 1925, 1754; Rec., 1924, 551; C. r., 1928, 1555; Abs. A., 1928, 1107.

**Cutting Hard Glass Tubing.**—To cut hard glass tubing a deep file mark is made at the desired length. Around the tube, one on each side of the file mark, are folded two strips of wet filter paper. These rolls of paper are moved to within 0·5 cm. of each other and bound on the tube by pieces of cord. The space between the rolls of paper is then heated in a small pointed blowpipe flame, directing the flame so as to strike only the top of the tube while the latter is turned. If the tube does not crack across at first, it is strongly heated, and a few drops of water from a tap allowed to fall on the file mark. This generally effects a neat cut.

## CHAPTER XXXV

### ESTIMATION OF NITROGBN

### Dumas Method (Macro)

THE substance is completely burned by **CuO** in a tube filled with $CO_2$; oxides of **N** are decomposed as before (reduced **Cu** spiral) and the **N** evolved is collected over **KOH**; while the **C** and **H**, being oxidised to $CO_2$ and $H_2O$ respectively, are retained by the **KOH** solution. Addition of $Ba(OH)_2$ to the last minimises frothing.

The combustion may be carried out in two ways: (*a*) in a tube sealed at one end, the $CO_2$ being generated from materials inside the tube, and (*b*) in a tube open at both ends, the $CO_2$ being generated in a second vessel or in a Kipp's apparatus of the Pregl type and passed into the combustion tube. Method (*a*) is the more convenient when estimations are conducted occasionally, and method (*b*) when estimations are frequently conducted.

*Method* (*a*).—500 gms. of wire-form and 100 gms. of powder **CuO** are placed in separate fireclay basins. The first is heated to a dull red heat in a muffle furnace, and the second over a Bunsen flame. While they are being heated the combustion tube is prepared.

A combustion tube 80—85 cms. long and similar to that used for the estimation of **C** and **H** is selected. A glass rod is sealed to one end and the tube is heated near this end in a blowpipe flame until the glass softens, when it is quickly drawn out and rounded as described on p. 42. When cold it is thoroughly washed out and dried.

The **CuO** is now allowed to cool somewhat before being introduced into two clean dry flasks, which are closed with ground-glass stoppers or corks coated with tinfoil.

When the tube is about to be filled it should be clamped in a vertical position at the side of the bench and at a suitable height for filling. A funnel with a short but wide stem should be inserted in the open end of the tube to assist in the filling.

As shown in Fig. 73, sufficient magnesite to fill 12—13 cms. is first placed in the tube; it should be in pieces the size of a pea, and sifted free from powder; dark or discoloured grains should be rejected. It is important to use only the best qualities of magnesite. A plug of asbestos or **Cu** gauze is then inserted and pushed home. Enough wire-form **CuO** is then poured in through the funnel to fill approximately 8 cms. of the tube; this is followed by a 2 cms. layer of **CuO** powder. For mixing the substance with **CuO** powder it is convenient to use a weighing bottle of such shape (**Fig. 74**) as enables it to be inserted in the end of the combustion

tube. Sufficient **CuO** powder to fill about 5 cms. of the combustion tube is placed in this bottle; about 0·2 gm. of the powdered substance to be analysed is accurately weighed out from another weighing bottle (which

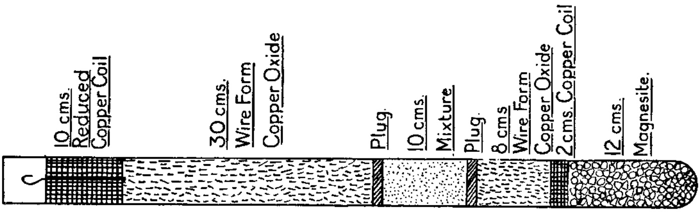



FIG. 73.

should contain the approximate quantity) and placed on top of the **CuO** in the first bottle; some more **CuO** powder, sufficient to cover the substance, is added and the whole gently mixed by shaking the bottle with stopper inserted. The contents are now poured into the combustion tube and the bottle rinsed a few times with **CuO** powder, the rinsings being poured into the combustion tube. The layer of **CuO** powder and substance should be approximately 10 cms. in length. A 30 cms. layer of wire-form **CuO** is then poured in and an asbestos plug inserted to keep it in position. A reduced **Cu** spiral, 10 cms. long, is prepared as described on p. 447; as in the estimation of **C** and **H** in nitrogenous compounds, it serves to decompose oxides of **N** with the liberation of free **N**; it is placed in position as shown in Fig. 73.

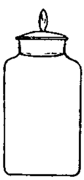


FIG. 74.

Before filling the tube the subdivisions should be marked off against a metre stick; the various lengths should not differ much from the figures given, as otherwise the layer of coarse **CuO** may be too short or the **Cu** spiral out of position. When the tube is filled, it is fitted with a good rubber stopper carrying a bent delivery tube, and while in a horizontal position on the bench is gently tapped along one side to make a passage for gas above its contents.

The tube is now placed in a furnace possessing a flame surface of 75 cms. The furnace should be tilted so that the sealed end of the tube is somewhat higher than the other, and the 5 cms. free space should just lie outside the furnace. This arrangement prevents any moisture which collects in the protruding part of the tube from running back into the heated portion. In order to protect the rubber stopper, a square of asbestos board, having a circular hole in the centre, is placed over the tube between the furnace and the stopper.

For the collection of the **N** a graduated nitrometer (Fig. 75) is used.

Into this a quantity of **Hg** sufficient to fill it 4—5 mms. above the entry tube is first placed. A solution prepared by dissolving 150 gms. of **KOH** and 3 gms. $\mathbf{Ba(OH)_2}$ in an equal weight of water in a porcelain dish is then poured into the pear-shaped reservoir. By opening the tap and raising the reservoir the apparatus becomes filled and should remain so

on closing the tap and lowering the reservoir. The tap should be greased and examined to see that it is thoroughly gas-tight. The entry tube of the nitrometer is connected to the delivery tube extending from the combustion tube by means of thick pressure rubber tubing on which a screw pinchcock is placed.

**The Combustion.**—The top of the nitrometer is opened and the pear-shaped reservoir lowered so that it contains practically all the **KOH** solution. The pinchcock is opened, leaving the apparatus ready for flooding with $CO_2$. The burners under one half of the magnesite layer at the sealed end of the tube are lit and gradually turned on until the flames all but meet over the tube; the tiles over these burners are then closed down. A rapid stream of $CO_2$ is thus produced, which quickly drives the air out of the tube.

After a rapid current of $CO_2$ has been evolved for 10 minutes, the

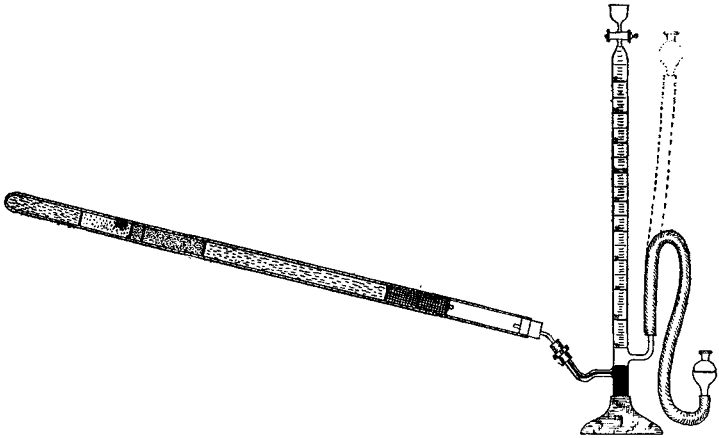


FIG. 75.

burners under the spiral and the layer of coarse oxide to within 10 cms. of the **CuO** powder are lit in order to drive out any occluded gases (**H** and air). In another 15 minutes the current of $CO_2$ is allowed to slacken a little; the nitrometer is filled with **KOH** solution by raising the reservoir and closing the tap.

The gas entering the nitrometer is now largely absorbed on passing up the column of **KOH**; the bubbles should decrease in size as they ascend, and appear as mere specks on approaching the top. If, however, this is not the case, owing to the combustion tube still containing an appreciable quantity of air, the tap should be opened and the reservoir lowered and a rapid current of $CO_2$ passed for 5 minutes longer. The test is again repeated; if after 2 minutes only a trace of foam has collected, the nitrometer is filled with **KOH** solution, the tap closed, and the reservoir lowered as far as possible. The current of $CO_2$ is lessened, all but one burner under the magnesite being either extinguished or lowered. The

**Cu** spiral and the part of the wire-form **CuO** already heated should now be at dull red heat. The burners under the wire-form **CuO** on both sides of the fine oxide are now lit, beginning with those farthest away from the substance and lighting two at a time—one on each side. Each burner, the tiles above it being closed, should heat the tube to a dull red heat before its neighbour is lit, but the flames should not meet above the tube. When the flames approach the fine oxide mixed with the substance the gas passing into the nitrometer should be carefully watched, and as soon as any **N** collects the further heating of the substance should be done very gradually. A little of the substance should be examined beforehand to ascertain whether it is easily volatile. If the substance is easily volatile it should be heated at first with very small flames or with hot tiles brought from an already heated part of the furnace. The success of the analysis depends on the gradual heating of the substance. Only one burner at a time should be lit under the substance, and when the amount of unabsorbed gas evolved at this heat slackens another burner is lit. The rate of gas bubbles passing up the nitrometer should not be greater than can be easily counted; irregular bursts of gas may cause the **KOH** solution to be sucked back into the combustion tube. When the substance, having been heated in this fashion to dull redness, ceases to evolve **N,** the burners under the magnesite layer are re-lit, and a not too rapid stream of $\mathbf{CO_2}$ passed through the apparatus for about 15 minutes in order to drive all traces of **N** into the nitrometer.

The absorption apparatus is then closed by the pinchcock and disconnected from the combustion apparatus at the rubber tubing. The burners under the spiral and oxide are gradually turned down so that the combustion tube cools with a slow stream of $\mathbf{CO_2}$ passing through it; this prevents the **Cu** spiral from being oxidised. The reservoir is raised until the liquid in it is at the same level as the liquid in the nitrometer, and a thermometer is hung beside the latter. The levels of the liquid in the reservoir and nitrometer are adjusted occasionally, and in about an hour the volume of **N** is read and the temperature and atmospheric pressure noted.

$$\%\mathbf{N} = \frac{\mathrm{V}(\mathrm{P} - p) \times 0{\cdot}04515}{(273 + t)w},$$

where $w$ is the weight in grams of the substance taken, V the observed volume of **N,** P the barometric pressure in mms. of **Hg**, and $p$ the vapour pressure of the **KOH** solution at the temperature $t$; when 50 per cent. **KOH** solution is used its vapour tension is negligibly small. For table of vapour pressures of **KOH** solutions, see p. 515.

*Method* (*b*).—The combustion tube is in every way similar to that used in connection with the estimation of **C** and **H.**

The short tube (Fig. 76) is partially filled with powdered $\mathbf{NaHCO_3}$ or magnesite in pieces the size of a pea, and a loose plug of glass wool is inserted to retain solid particles; the tube should be tapped horizontally to provide a channel for gas; it is heated either in a short furnace or by

flat flame Bunsen burners. The two tubes are connected by rubber stoppers and a trap which prevents any drops of moisture arising from the decomposition of the bicarbonate from passing into the heated combustion tube. The method of filling the combustion tube is indicated in the general diagram (Fig. 76). The mixture of fine **CuO** and substance is placed in a long boat made of porcelain, quartz or **Cu,** or directly into the combustion tube along with the **CuO** powder as described in (*a*). The **CuO** spiral takes the place of the short layer of **CuO** mentioned in method (*a*) and serves to oxidise any vapours which diffuse backwards. The reduced **Cu** spiral is inserted after the rest of the tube is filled. The manner of connecting the combustion tube to the nitrometer as well as the method of conducting the combustion is the same as described in method (*a*). It is particularly important that the evolution of $\mathbf{CO_2}$ from the smaller tube should not cease at any time, since otherwise vapours may diffuse backwards into the trap.

The convenience of this method for carrying out a number of consecutive estimations is obvious ; the spirals can be quickly removed, treated and replaced, and the short tube can be quickly recharged and connected. Before starting a second combustion, however, the boat and the reduced

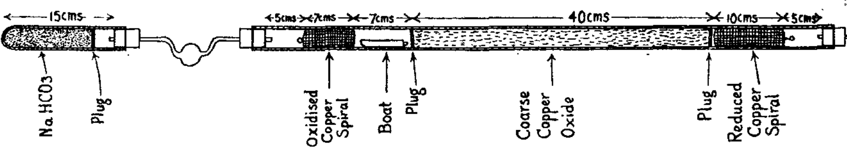



FIG. 76.

**Cu** spiral should be removed from the tube and a current of **O** passed through while the tube is heated to dull redness for about 15 minutes ; any reduced **Cu** is thus re-oxidised. After this preliminary heating the tube should be allowed to cool in a current of $\mathbf{CO_2}$ generated from a Kipp's apparatus. **CuO**, which occludes a small quantity of air when heated and cooled in air, does not occlude the gas so readily when cooled in $\mathbf{CO_2}$. $\mathbf{CO_2}$ may also be obtained by the action of acid on marble in a Kipp's apparatus ; the marble must first be boiled in water and cooled alternately several times to expel occluded air, and even then it is difficult to get rid of the last traces. In a few cases the method gives results which are too high owing to the formation of $\mathbf{CH_4}$, which is not completely oxidised by **CuO** in absence of **O,** and collects in the nitrometer. To obviate this difficulty the wire-form **CuO** should be replaced by a long layer of $\mathbf{PbCrO_4}$ and the substance mixed with fine **CuO** and powdered $\mathbf{PbCrO_4}$ (J. C. S., 89, 570 ; see also J. S. C. I., 49, 447). If any **NO** escapes decomposition by the reduced **Cu** spiral its presence is detected by the formation of red fumes when the gas in the nitrometer is mixed with air.

*Note.*—**N** as **NO** occupies twice the volume of the same amount of **N** in the free state.

## Dumas Method (Micro Modification)

The Dumas micro method for the estimation is very similar to the ordinary macro method. The micro nitrometer has a graduated capacity of 1·5 c.cs. In the combustion tube the filling is wire-form **CuO** alone, and instead of a removable **Cu** gauze spiral a portion of the **CuO** filling at the snout end of the tube is reduced *in situ* with a current of **H.** The $CO_2$ can be generated from a Kipp's apparatus, precautions being taken to expel all air ; some workers, however, prefer to obtain the $CO_2$ by heating pure $NaHCO_3$ in a hard glass tube.

The $CO_2$ for the estimation can be generated by the action of dilute $H_2SO_4$ on $Na_2CO_3$ in a special apparatus. (See Lindenfeld (Abs. A., 1935, 369) or Price and Twiss, Practical Organic Chemistry, p. 162.) The main difficulty in the micro and hemi-macro Dumas methods is the problem of getting all the air out of the $CO_2$ supply. The substance is weighed directly into the combustion tube from a micro weighing bottle and washed down with previously ignited **CuO** powder. The nitrometer is charged with 40 per cent. **KOH** solution to which has been added a small amount of $Ba(OH)_2$ to prevent frothing. In view of the small volume of the nitrometer, allowance must be made for the volume of liquid adhering to the wall after the combustion is finished. Factors are given for this in Pregl's book. Once the technique is acquired, the method will be found rapid and reliable.

## Dumas Method (Hemi-macro Modification)

The following method for the estimation of **N** can be utilised for amounts of substance varying from 20—60 mgs. (according to the percentage of **N**). The combustion tube is snout-ended and of the type and size described in J. S. C. I., 1935, 46T. A loosely packed Gooch asbestos plug is placed in the snout, then a filling of wire-form **CuO** held in place by a short oxidised **Cu** gauze plug (total length, 25 cms.), followed by a reduced **Cu** gauze spiral (9 cms.), then the boat, the filling being completed with an oxidised **Cu** gauze spiral. (See also Bobranski and Sucharda, *loc. cit.*, p. 29.)

The nitrometer is of the shape described by Pregl and is graduated in 0·05 c.c. divisions for 10 c.cs. 50 per cent. **KOH** with the addition of a small amount of $Ba(OH)_2$ (to prevent frothing) is used. The $CO_2$ is supplied from a Kipp's apparatus, modified along the lines recommended by Pregl.

In this method the substance is either placed in a boat or inserted from a weighing bottle along with **CuO** powder. If a boat is used it should be filled to the brim with ignited **CuO** powder and placed in the tube next to the reduced **Cu** spiral. A rapid stream of $CO_2$ is blown through the tube to remove air. The **CuO** end of the tube is heated and the stream of $CO_2$ cut down to as slow a rate as possible with safety. This rate must be determined by practical experiment. If it is too quick, then the blank will show a fairly large amount of air out of proportion to the volume of **N** to be measured. On the other hand, if the rate is too slow, a suck-back

into the tube may occur. The time for combustion will also be increased. A rate of about one bubble per second is usually satisfactory. A blank determination is made for 10 minutes to determine how much air is passing through the tube (this is subtracted, in proportion to the time taken for the combustion proper, from the volume of gas in the nitrometer after the experiment). The small amount of air is removed from the nitrometer, and the reduced **Cu** spiral heated. At the same time the oxidised spiral beyond the boat is heated and the substance distilled steadily and regularly from the boat. It is essential that this be done slowly, otherwise there is a tendency for **CO** and $CH_4$ to be formed and the result will be too high. Heating is continued until evolution of **N** ceases. The nitrometer is then detached and taken to another room to cool (20 minutes). It is advisable to run in some fresh **KOH** solution from the top of the nitrometer before reading the volume. A reduction of 1 per cent. of the volume is made to compensate for liquid adhering to the wall of the nitrometer.

While the combustion tube is still hot the reduced spiral should be removed and again reduced. A current of **O** or air should also be passed through the heated tube in order to re-oxidise the filling.

The time of combustion varies from substance to substance. The blank determination occupies 10 minutes, and the combustion proper 15—30 minutes.

## Kjeldahl Method

Compounds which contain **N** can usually be oxidised by heating with conc. $H_2SO_4$, the **C** being converted into $CO_2$, and the **N** to $(NH_4)_2SO_4$. $NH_3$ can then be liberated from this solution and estimated.

0·5—5 gms. of the substance are weighed into a long-necked round-bottomed Kjeldahl flask of 300—500 c.cs. capacity, and 20—30 c.cs. of pure conc. $H_2SO_4$ added by means of a pipette. 10—20 gms. of pure $KHSO_4$ (or anhydrous $K_2SO_4$) and 0·2 gm. **Se** are then added, and the contents of the flask heated over a sand bath or small Bunsen flame until almost boiling. The neck of the flask can be partially closed with a loose-fitting, short-stemmed, glass funnel. On further heating the dark-coloured mass grows lighter until finally it is colourless, or only a faint straw colour.

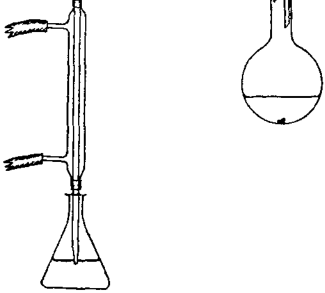


FIG. 77.

The contents of the flask are then washed into the distilling flask of an ammonia estimation apparatus (Fig. 77) with successive small amounts of distilled water. The $NH_3$ is then determined in the usual manner.

An alternative form of ammonia distillation apparatus, Fig. 78, is due

to Stock (Abs. A., 1892, 1516). The flask A contains the partially neutralised solution of $(NH_4)_2SO_4$. Through the rubber stopper the stem of a dropping funnel containing conc. **NaOH** solution passes. This flask is attached to a second flask B by a glass connecting tube. The flask B contains distilled water, which is kept boiling vigorously during distillation. A delivery tube from flask B connects with the condenser C. The other end of the condenser tube passes through one hole in a rubber stopper into a wide-mouthed conical flask D. A second hole in the stopper carries a glass tube connection leading to the U-tube E (alternatively the end of the condenser may pass through a single-bored stopper

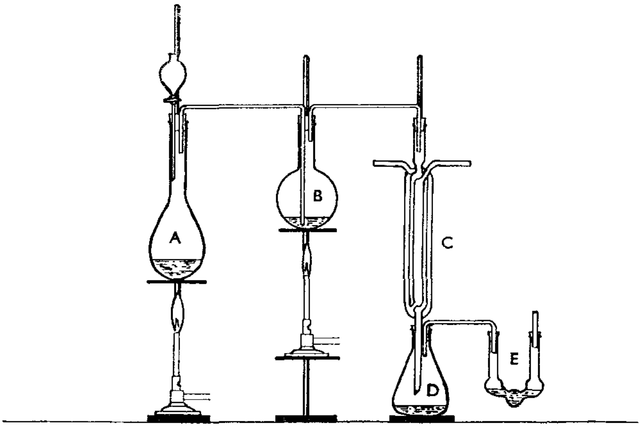



FIG. 78.

into a filter flask, and the U-tube E can be attached to the suction tube of this flask). 50 c.cs. of standardised $H_2SO_4$ solution are distributed between the flask D and the U-tube E. A small amount of methyl-red indicator is placed in E.

A few pieces of pure **Zn** foil, and excess of alkali from the dropping funnel are added to A, the contents of which are gradually heated to boiling. The vapour passes into the trap flask B, the contents of which are kept boiling, and the $NH_3$ distils from this flask into the receiver D. The unchanged acid is titrated in the usual manner.

$$\% \mathbf{N} = \frac{\text{vol. of } \frac{N}{2} \text{ acid neutralised} \times 0{\cdot}7}{\text{wt. of substance taken}} \text{ (if } \frac{N}{2} \text{ acid used).}$$

**Catalytic Method.**—An interesting and more or less generally useful method has been described by Ter Meulen (Rec., 1930, 49, 396; 1934, 53, 118; Bl., 1935, (v), 2, 506). The method consists of heating the substance in a boat with nickel-thoria catalyst in a stream of **H** and passing the vapour through asbestos impregnated with **Ni.** The **N** emerges in the form of $NH_3$, which is trapped in standardised N/20 $H_2SO_4$ and estimated. See also Ter Meulen and Heslinga, "Nouvelles Methodes d'Analyse Chimique Organique," 2nd ed., Paris, Dunod.

# CHAPTER XXXVI

## ESTIMATION OF HALOGENS AND SULPHUR

### (A) Halogens

(*a*) **Carius Method.**—The method of Carius, which is applicable to practically all types of organic halogen compounds, consists in oxidising the substance with fuming $\mathbf{HNO_3}$, under pressure in presence of $\mathbf{AgNO_3}$. The silver halide formed is then separated by filtration and weighed.

The following are required for the analysis :—

1. A tube of thick-walled soft glass, about 50 cms. long, 12—13 mms. inside diameter, and walls 2—3 mms. thick. Tubes of hard potash glass with walls 2 mms. thick may also be used. The tube is carefully sealed at one end, in the manner described on p. 41, after which it is thoroughly washed and dried.

2. A weighing tube, about 10 cms. long, sealed at one end and of such a diameter that it slips easily into the thick-walled tube.

3. A funnel tube or thistle funnel, about 40 cms. long, which fits into the sealed tube and serves to convey the $\mathbf{AgNO_3}$ and fuming $\mathbf{HNO_3}$ to the bottom of this tube.

4. Pure fuming $\mathbf{HNO_3}$, the purity of which should be tested by diluting 2 c.c. of it with 50 c.cs. of distilled water and adding a few drops of $\mathbf{AgNO_3}$ solution. The liquid should remain perfectly clear. If it contains **Cl** it must be redistilled over a few crystals of $\mathbf{AgNO_3}$.

5. A tube furnace (bomb furnace). (See p. 43.)

6. Solid $\mathbf{AgNO_3}$.

**Filling and Sealing the Tube.**—The exact weight of the weighing tube is determined. Into it is placed about 0·2—0·3 gm. of the finely powdered substance to be analysed, and the tube plus its contents exactly weighed again. By means of the funnel tube a quantity of finely powdered $\mathbf{AgNO_3}$ varying from 0·5—1 gm., according to the percentage of halogen, is introduced into the sealed tube. This is followed by 2 c.cs. of fuming $\mathbf{HNO_3}$. The funnel tube is then removed, care being taken not to touch the sides of the sealed tube with it, and, while the latter is held at a slight angle, the weighing tube is allowed to slide gently down to the bottom, but the substance must not come into contact with the acid. The open end of the tube is then sealed in the blowpipe, as described on p. 41, care being taken that during the sealing the acid does not gain entrance to the weighing tube.

When the substance to be analysed is a liquid, it is placed in a bulb tube with an open capillary, which is introduced, bulb foremost, into the tube after the $\mathbf{AgNO_3}$ and $\mathbf{HNO_3}$ have been inserted.

**Heating the Tube.**—When cold, the tube is placed in an iron protecting cylinder with a screw cap and the cylinder transferred to a tube furnace, where it is heated according to the directions given on p. 43. The temperature and duration of heating depend on the resistance of the substance towards decomposition. With many compounds that oxidise easily, 2—4 hours at 150°—200° is sufficient, while substances which do not easily oxidise, especially those containing **S**, must be heated 8—10 hours and as high as 250°—300°. It is advisable to commence the operation in the morning and to raise the temperature gradually to 200° during the first 4 hours, and to 250°—300° during the second period of 4 hours. Practically all substances are decomposed by this treatment. For any particular substance, experiment will show whether the duration of heating and the temperature can be modified.

**Opening the Sealed Tube.**—The tube is allowed to remain in the furnace until perfectly cold. The cylinder containing the tube is then removed from the furnace and the capillary end of the tube allowed to project 3 or 4 cms. Before softening the capillary in a large flame, care should be taken to drive back into the tube by gently heating over a small flame any liquid which may have collected in the capillary.

Full directions are given on p. 44 for opening the capillary. After opening the capillary the tube is removed from the case and examined to see if it still contains crystals or oily drops of the undecomposed substance. If it does, the capillary is again sealed and the tube reheated in the furnace; but if it does not, a deep file scratch is made in the wide part of the tube, about 3 cms. below the shoulder of the capillary, and the end broken off according to the second method of opening sealed tubes (p. 44).

The tube is then held in a slanting position and the conical end removed; any fragments of broken glass are carefully wiped off and not allowed to become admixed with the contents of the tube. The detached part is washed free from any liquid or precipitate which may have adhered to it with distilled water into a beaker. The contents of the tube are diluted with distilled water and added to the beaker, care being taken that the fall of the weighing tube does not injure the vessel. The tube is held in an inverted position over the beaker and the outer edges of the open end washed with distilled water. The precipitate still remaining in the tube is washed out by repeated shakings with small quantities of distilled water. Any precipitate which is attached to the tube is loosened by rubbing with a long piece of glass rod over the end of which is placed a short piece of rubber tubing. The short end of a thin piece of glass rod, bent at a right angle, is then inserted in the mouth of the weighing tube and, while the latter is removed just above the surface of the liquid, the outside is washed with distilled water. It is then held in the fingers and any precipitate inside washed with distilled water into the beaker. The silver halide is then estimated after filtering through a Gooch crucible, as in inorganic analysis.

(*b*) **Bacon's Modification of Stepanoff's Method.**—This method can be

usefully employed with many different types of organic compounds. The substance is heated in alcoholic solution with excess of sodium, when decomposition ensues according to the scheme—

$$RX + C_2H_5OH + 2Na = RH + NaX + C_2H_5ONa.$$

The sodium halide can be separated and estimated either volumetrically or gravimetrically by recognised methods.

The amount of reactants employed depends on the halogen present. For a weight W of substance the following relationships approximately hold :—

| Wt. of substance W. | Wt. of Alcohol 98—99%. | Wt. of Na. |
|---|---|---|
| Chloro compound . . | 160 W. | 20 W. |
| Bromo compound . . | 70 W. | 9 W. |
| Iodo compound . . | 45 W. | 6 W. |

The substance (0·2—0·5 gm.) is weighed in a short wide tube (too narrow a tube should be avoided as substance may remain undissolved). The calculated amount of alcohol is then put in a round-bottomed flask (250—400 c.cs.) fitted with a reflux condenser and the tube containing the substance introduced. Small pieces of sodium (see p. 508) are dropped down the condenser into the flask. The action is fairly vigorous at first and is completed by gently heating towards the end for 30—60 minutes. After cooling, the contents of the flask are washed carefully with distilled water into a porcelain basin or beaker and almost neutralised by the addition of dilute $\mathbf{HNO_3}$. The slightly alkaline solution is warmed for some time on the water bath to remove alcohol, cooled and excess of $\mathbf{HNO_3}$ added. A resin often separates at this stage, but it is removed by filtration and washed to remove adhering sodium halide. The filtrate and washings are united and excess of $\mathbf{AgNO_3}$ solution added. The silver halide is isolated and weighed or determined volumetrically.

**Piria and Schiff's Method.**—This method is only applicable to those organic substances which are not highly volatile. Liquids which combine directly with **CaO** or $\mathbf{Na_2CO_3}$ may also be analysed in this way.

About 0·1—0·3 gm. of the substance is weighed into a very small platinum crucible, which is then filled up with an intimate mixture of anhydrous $\mathbf{Na_2CO_3}$ (1 part) and pure powdered **CaO** (4—5 parts). The crucible is then placed in an inverted position in a larger platinum crucible, the space between the two being completely filled with the same mixture of $\mathbf{Na_2CO_3}$ and **CaO**, so that the small crucible is entirely covered.

The outer crucible is now heated in a large Bunsen or blowpipe flame so that the outer portions attain a high temperature before the substance in the smaller crucible begins to decompose. The whole is finally raised to a red heat. The crucibles and contents are allowed to cool, then digested with water in a strong beaker. Dilute $\mathbf{HNO_3}$ is cautiously added

until the solution reacts acidic, care being taken that the temperature does not rise to any extent. External cooling is advisable. The solution is filtered to remove any carbonaceous matter and the halogen precipitated with $\mathbf{AgNO_3}$ and estimated as described in the Carius method. When the substance contains **I** the method requires modification; $\mathbf{Na_2CO_3}$ is then employed alone, as $\mathbf{Ca(IO_3)_2}$ would be formed were **CaO** present. If any **I** appears after acidification with $\mathbf{HNO_3}$ it is reduced to **HI** with the minimum quantity of $\mathbf{H_2SO_3}$.

## (B) Sulphur

**Carius Method.**—The procedure is almost the same as that described for the estimation of halogens. The compound is oxidised in a sealed tube with fuming $\mathbf{HNO_3}$, but neither $\mathbf{AgNO_3}$ nor $\mathbf{BaCl_2}$ is placed in the tube. The resulting $\mathbf{H_2SO_4}$ is precipitated and weighed as $\mathbf{BaSO_4}$. Similar quantities of substance and of fuming $\mathbf{HNO_3}$ are taken, and the processes of sealing, heating and opening the tube are conducted in the same way as for halogens. The contents of the tube, after being washed into a beaker, are filtered free from fragments of glass. The filtrate is diluted to about 300 c.cs. with water, heated to boiling, and the $\mathbf{H_2SO_4}$ precipitated as $\mathbf{BaSO_4}$ by the addition of $\mathbf{BaCl_2}$ solution. A large excess of $\mathbf{BaCl_2}$ should not be added owing to the sparing solubility of $\mathbf{Ba(NO_3)_2}$ in aqueous mineral acids; this can be avoided by allowing the precipitate to settle before adding more of the solution. The liquid is heated over a small flame until (sometimes 1—2 hours) the precipitate settles and the supernatant liquid is clear. It is then filtered either through an ordinary funnel or through a Gooch crucible, and the precipitate washed well with hot water. The weight of $\mathbf{BaSO_4}$ is finally determined.

$$\% \, \mathbf{S} = \frac{\text{wt. of } \mathbf{BaSO_4} \times 13{\cdot}7339}{\text{wt. of substance taken}}.$$

Frequently in this method a considerable amount of gas is evolved and the tube is liable to burst. In such cases the sealed tube should be heated only to 200° for 2 hours, after which it is allowed to cool and the capillary carefully opened (p. 44) to allow the gases to escape. It is then resealed and heated to 300°.

Many **S** compounds, especially aliphatic sulphides, do not give accurate results, since the sulphones formed by the action of $\mathbf{HNO_3}$ are generally so stable as to resist further decomposition by the acid. When stable sulphones are formed the contents should be washed out into a nickel basin, made alkaline with **KOH**, and evaporated to dryness. The residue is then treated as described in the fusion method.

**Fusion Method.**—This method is applicable only to substances which are not easily volatile.

About 6 gms. of $\mathbf{Na_2O_2}$ are heated in a crucible immersed in a sand bath (the temperature of which may be taken with a thermometer bulb immersed in the sand) to about 150° for about 15 minutes in order to expel

absorbed $H_2O$. After cooling, the peroxide is removed and finely powdered. A quantity of the substance, 0·2—0·4 gm., is intimately mixed with 4 gms. of the dried $Na_2O_2$ and 7 gms. $Na_2CO_3$ in an iron crucible. It is heated very cautiously with a small flame which does not touch the crucible at first. The flame is very gradually increased until the crucible is ultimately raised to a red heat, at which it is maintained for 30 minutes. (*Note.*—Great care is necessary in the early stages of the heating in order to avoid explosive reaction.)

The melt is allowed to cool, taking care to avoid loss of any material which may have crept up the sides of the crucible. It is then digested with $H_2O$, a few c.cs. of **Br** water added, and the resulting solution with the crucible and lid in it warmed on the water bath for 30 minutes. The crucible and lid are then removed, washed thoroughly, and the solution acidified with **HCl** and filtered. The **S** in the filtrate is finally precipitated and estimated as $BaSO_4$. The purest reagents available should be employed and a blank determination performed.

**Simultaneous Determination of Halogens and S.**—The operation is conducted as described under the Estimation of Halogens (Carius). The sealed tube is charged with $AgNO_3$, fuming $HNO_3$ and substance. After the heating the silver halide is filtered and estimated. The filtrate, which contains the excess of $AgNO_3$ in addition to the $H_2SO_4$ formed by oxidation, is warmed, and to it is added a boiling solution of $Ba(NO_3)_2$ (free from chloride). The solution should be very dilute—about 500 c.cs. for 0·3—0·4 gm. substance originally taken—and an excess of $Ba(NO_3)_2$, owing to its sparing solubility, is to be avoided. The $BaSO_4$ is estimated as described under determination of **S.**

The Carius method can be worked on a micro (see Pregl, *loc. cit.*) or hemi-macro scale. Halogens can be estimated by other methods (see, *inter alia*, Bobranski and Sucharda, *loc. cit.*) in which the substance is completely oxidised in the dry state, **Cl** and **Br** being trapped in solid $BaCO_3$, **I** in $Na_2SO_3$ in a special apparatus.

Oxidation methods for the estimation of **S** are in process of development and are outside the scope of this book. Ter Meulen (*loc. cit.*) estimates **S** in organic compounds by catalytic reduction to $H_2S$.

# CHAPTER XXXVII

## Determination of the Equivalent of an Acid

*By Titration with Standard Alkali.*—$\frac{N}{10}$ aqueous and alcoholic potash as well as $\frac{N}{10}$ baryta solution are used for titrating organic acids, phenolphthalein being in all cases the best indicator. Baryta solution is the most suitable alkali since it can be prepared and kept free from carbonate. The baryta solution is contained in the apparatus, Fig. 79. The storage bottle is connected to the top and bottom of a burette having a 2-way stopcock, and the baryta solution is protected from atmospheric carbon dioxide by a soda-lime tube inserted through the cork in the top of the storage bottle.

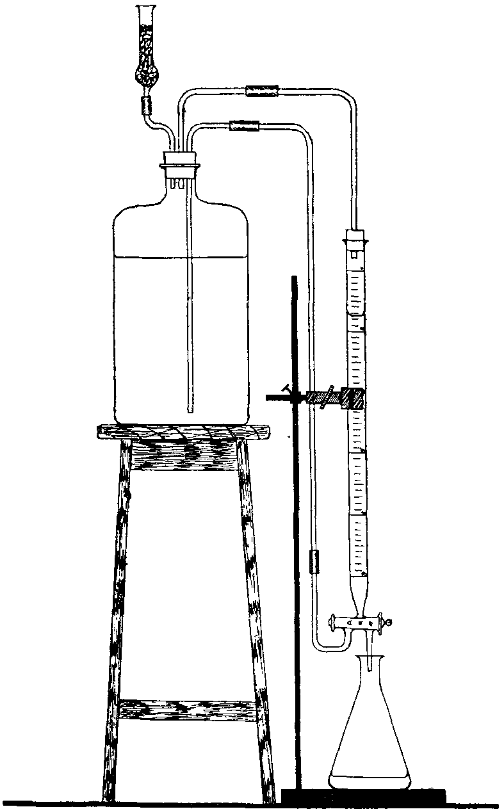


FIG. 79.

The baryta solution is prepared from pure crystalline barium hydroxide, $Ba(OH)_2.8H_2O$, by dissolving in distilled water. Any carbonate is allowed to subside and the clear supernatant liquor syphoned into the storage bottle after the latter has been filled with air free from carbon dioxide.

To determine the equivalent of an acid, a suitable quantity of it—determined by trial titrations—is dissolved in distilled water if soluble in water, and if insoluble in water in aqueous alcohol, or in alcohol free from acid. The average of a few readings which should agree to within 0·5% is taken, and the amount of acid necessary to neutralise 85·5 gms. of barium hydroxide calculated.

*Preparation and Analysis of Silver Salts.*—The preparation of metallic salts and their analysis is the chief method of determining equivalents of organic acids. Salts of silver, calcium, barium, sodium, or potassium may be used, and a few preliminary tests will reveal which salt is the most suitable. Generally the silver salt, when sparingly soluble in water, is selected, since its isolation, purification, and decomposition can be readily effected. Silver salts of organic acids usually crystallise without water of crystallisation, but some have the disadvantage of being easily attacked by light.

A small quantity of the acid is neutralised with pure aqueous ammonia, and the excess of the latter boiled off. Sufficient silver nitrate is then added and the liquid cooled. Crystals of the sparingly soluble silver salt separate and are filtered off. These are recrystallised when possible from hot water, collected, well washed, dried in a steam oven for 30 minutes and allowed to cool in a vacuum desiccator. 0·2—0·3 gm. of the dry silver salt is weighed into a porcelain crucible and gently ignited until all organic matter is destroyed, and until the crucible containing the residue of silver is of constant weight—care being taken that heat is not applied too strongly, since silver is volatile at a high temperature.

$$\text{The equivalent of the acid} = 108\left(\frac{\text{wt. of silver salt}}{\text{wt. of silver}} - 1\right)$$

$$\text{and the M.W., when monobasic} = 108\,\frac{\text{wt. of silver salt}}{\text{wt. of silver}} - 107.$$

When the silver salt of an acid is soluble, the calcium or barium salt may be employed. These are prepared either by adding a soluble calcium or barium salt to a soluble salt of the acid, or by neutralising the acid itself with pure lime or baryta water. Ignition of a calcium salt is carried out either gently to the carbonate, or strongly to the oxide. A barium salt is first ignited until decomposition of organic matter is complete, then cooled and converted into the sulphate by addition of a few drops of conc. sulphuric acid, and finally ignited as sulphate. Calcium and barium salts often contain water of crystallisation and hence may require great care in drying.

When the sodium or potassium salt is available in a pure state, a known weight is ignited until only a residue of pure carbonate remains. A few drops of conc. sulphuric acid are then carefully added, and heat from a small flame applied until the excess of sulphuric acid is driven off. If any specks of carbon remain the last process is repeated. Finally the residue is weighed as alkali sulphate.

When an acid contains halogen, and the silver salt method is employed, the residue after ignition is treated with a few drops of nitric acid and a little ammonium halide to ensure complete conversion into silver halide.

## Determination of the Equivalent of a Base

*By Titration.*—A crystalline salt of the base with some mineral or organic acid is prepared and purified, and the acid present in a weighed

quantity of the salt titrated with standard alkali (preferably baryta solution, p. 474) in presence of phenolphthalein. From the average of several readings the amount of the salt which contains one equivalent of the acid is calculated, and from this is subtracted the weight of one equivalent of the acid, leaving the weight of one equivalent of the base.

*Preparation and Decomposition of the Platinichloride.*—Most organic bases form well-defined crystalline double salts with platinic and auric chlorides of the general formulæ $B_2H_2PtCl_6$ and $B_2H_2AuCl_4$, where B represents one equivalent of the base. (Iridio-chlorides and cuprichlorides are sometimes used.) These salts are prepared by adding platinic or auric chloride to a solution of the base in dilute hydrochloric acid. The double salt is filtered off, recrystallised (generally from alcohol), and dried on a porous plate in a vacuum desiccator. When dry, a weighed quantity (0·5—1·0 gm.) is heated in a porcelain crucible, gently at first with the lid on, and afterwards strongly until all organic matter is burnt away. The residue is weighed as platinum or gold. Taking a platinum salt as example, the equivalent weight of the base is calculated as follows :—

$$\text{Molecular weight of the double salt} = \frac{\text{wt. of salt taken} \times 195}{\text{wt. of platinum residue}}.$$

M.W. of the salt — 409·9 (*i.e.*, M.W. of $\mathbf{H_2PtCl_6}$) = twice the equivalent of the base.

## Determination of Molecular Weight

**Rast's Method.**—This method is easily carried out, using an ordinary thermometer graduated in 0·5°, and gives results accurate to within 5%. It is not applicable to compounds which are not freely soluble in camphor or which react therewith or which decompose under the conditions. (B., 55, 1051, 3727.)

The method depends on the very high molecular constant (400) shown by camphor.

6—10 mgs. of the substance are accurately weighed and placed with about ten times the weight of pure camphor in a small, carefully cleaned test tube, which is sealed off and heated over a small flame until the contents melt. The melt is allowed to solidify, the tube is broken, and the contents (freed from glass) ground on a watch-glass or agate mortar. A small portion is placed in a thin-walled, wide melting point tube, pressed down with a thin glass rod, and heated to melting in the usual melting point apparatus. It is then allowed to cool until some crystals separate. After this, heating is conducted slowly and the temperature noted to within 0·5°, when the last crystal of camphor disappears. This is the freezing point of the solution. The freezing point of camphor is determined under the same conditions, using the same thermometer. The molecular weight (M) is given by the equation :

$$M = \frac{K \times w \times 100}{W \times d}$$

where w = weight of substance
W = " " camphor
d = difference in freezing point of camphor and that of mixture.
K = molecular depression constant for camphor.

The Molecular Depression Constant (K) for camphor is determined by using a substance of known molecular weight, say, naphthalene, and applying the following formula :

$$K = \frac{d \times M \times W}{w \times 100}.$$

The determination of this constant should precede that of each molecular weight.

# CHAPTER XXXVIII

## GROUP ESTIMATIONS

### Estimation of Primary or Secondary Amines by Acetylation

THE primary aromatic amines are most readily estimated by means of nitrous acid (see p. 493). Primary or secondary amines, either alone or in presence of tertiary amines, may be estimated by acetylation, since the last do not react. About 1 gm. of the substance or mixture is weighed into a small flask provided with a reflux air condenser, and 5 c.cs. of acetic anhydride added from a pipette having a soda-lime guard tube. In another flask, also provided with a similar condenser, 5 c.cs. acetic anhydride are placed. The two flasks are allowed to stand at room temperature for 30 minutes to 1 hour, after which time 50 c.cs. of water are added to each, and both are placed on the steam bath for an hour in order to convert the remaining acetic anhydride into acetic acid. After cooling, the amount of acetic acid in each flask is titrated with standard sodium hydroxide or standard baryta, using phenolphthalein as indicator. The difference in the two titrations corresponds to the amount of primary or secondary amine present.

$$2R.NH_2 + (CH_3CO)_2O = 2R.NH.COCH_3 + H_2O$$
$$2R.NH.R_1 + (CH_3CO)_2O = 2R.NR_1.CO.CH_3 + H_2O$$

The blank experiment is necessary since it is difficult to obtain acetic anhydride in a pure state, and also since there is a slight loss of this reagent from the apparatus during the operation. (For Xylene Modification, see C. Z., 17, 465.)

### Estimation of the Number of Hydroxyl Groups in a Compound

The acetyl derivative (each hydroxyl group acetylated) is prepared and purified, and a weighed quantity of it hydrolysed with benzene sulphonic acid. The acetic acid liberated is separated by steam distillation and titrated with baryta solution.

A solution of pure benzene sulphonic acid is prepared as follows :—

100 gms. of barium benzene sulphonate $(C_6H_5SO_3)_2Ba$ are recrystallised twice from distilled water. 50 gms. of the dry purified salt are then subjected to steam distillation until the distillate is no longer acid to litmus, small amounts of volatile impurities which are generally present in the barium salt being thereby removed. To the hot liquid is added the requisite amount (avoiding excess) of pure sulphuric acid necessary to convert the barium salt into barium sulphate and benzene sulphonic acid. The barium sulphate is filtered off and washed, and the filtrate and washings made up with water to give a 10% solution of the acid.

*Example.*—**Mannitol.**—The hexa-acetyl derivative (p. 259) is prepared and purified, and a quantity of it—about 0·2 gm.—along with 100 c.cs. of 10% benzene sulphonic acid solution placed in a steam distillation flask. The flask is connected to a condenser on one side and to an apparatus for the generation of pure steam on the other. A suction flask to serve as receiver is attached by a cork to the condenser, and to the side tube of the suction flask a soda-lime tube to prevent the entrance of carbon dioxide is attached. Steam is blown through the flask until (1·5—3 hours) the distillate passing over is neutral. The whole distillate is then titrated with standard baryta, using phenolphthalein as indicator.

*General Calculation.*—

$$W = \text{weight of acetyl compound}$$
$$w = \quad ,, \quad ,, \ \text{acetic acid (by titration)}$$
$$\frac{w \times 17}{60} = \quad ,, \quad ,, \ \text{OH} = a$$
$$W - \frac{w \times 42}{60} = \quad ,, \quad ,, \ \text{corresponding OH compound} = b.$$

Then $\frac{a}{b} \times 100 =$ percentage OH

also $\frac{a}{b} \times \frac{M}{17} =$ number of OH groups

where $M =$ molecular weight of OH compound.

It is obvious that this method serves for the estimation of acetyl groups present in esters of alcohols or phenols. It also serves for the estimation of acetyl groups present in substituted primary or secondary amines.

Many phenols are more conveniently estimated by "coupling" (see p. 494).

## Estimation of Acyl Derivatives

When the substance under estimation is either an acyl derivative of an alcohol or phenol which is not affected by alkali and air, or an acyl derivative of a volatile base, the estimation may be carried out as for esters with alcoholic potash (p. 509), any free base being removed by distillation before titrating the excess of alkali.

$$R.O.COR_1 + KOH = R.OH + R_1COOK$$
$$R.NH.COR_1 + KOH = R.NH_2 + R_1COOK.$$

When alcoholic potash cannot be employed, the acyl derivative may be hydrolysed with benzene sulphonic acid (see above) or phosphoric acid, provided that the acid produced is volatile in steam ; benzene sulphonic acid is a stronger acid than phosphoric.

## Estimation of Methoxyl or Ethoxyl Groups

All the usual determinations of these groups are based on the original method of Zeisel, which consists in decomposing the substance with hydriodic acid thus :—

$$R.(OCH_3)x + xHI = R(OH)x + xCH_3I.$$

The resulting methyl (or ethyl) iodide is converted into silver iodide by the action of alcoholic silver nitrate, and the number of methoxyl (or ethoxyl) groups calculated from the weight of silver iodide formed.

The hydriodic acid used is purified as described on p. 506, selecting for the determination the fraction of constant B.P. 127° and D. 1·68. The alcoholic silver nitrate, which is prepared by dissolving 4 gms. of silver nitrate in 10 c.cs. of water and adding 90 c.cs. of absolute alcohol, is preserved in a well-stoppered bottle in the dark, and should be filtered and acidified with one drop of nitric acid immediately before use.

A reliable modification of the process for the estimation of methoxyl is that of the British Pharmacopœia, 1932. The apparatus is shown in Fig. 80. A Pyrex flask (A) of about 100 c.cs. capacity, having a bulb (B) of about 70 c.cs. capacity blown on the side tube, contains the mixture of substance (about 0·2 gm.) and hydriodic acid (10 c.cs.). The side tube is connected through a smaller bulbed tube (C) to a set of bulbs (D, see Fig. 65), immersed in a water bath at 60° (95° for ethoxyl), containing red phosphorus suspended in a 2% aqueous solution of cadmium sulphate. To this is attached two absorption flasks (E), each containing about 20 c.cs. of the above alcoholic silver nitrate. To the flask (A) is

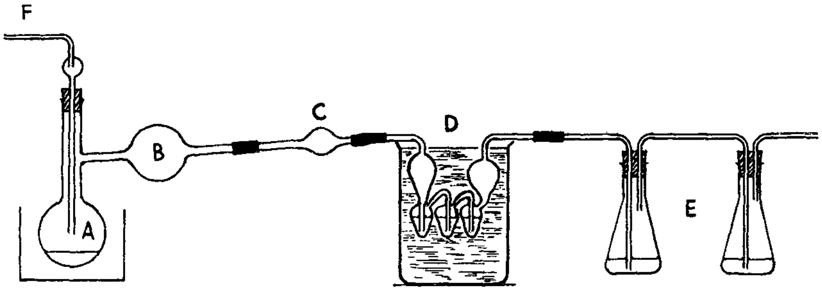



Fig. 80.

attached a side tube (F) through which carbon dioxide passes to within a short distance of the surface of the reacting mixture. (Care should be taken to bring all glass connections into contact within the rubber tubes.)

Carbon dioxide generated by interaction of sodium carbonate solution and dilute sulphuric acid and dried by passage through conc. sulphuric acid is delivered to the flask, which is maintained in a glycerine or metal bath at 140° for at least one hour until no further precipitate appears in the absorption flasks (E). (The mixture in the bulbs (D) absorbs iodine and hydriodic acid.) The silver nitrate flasks are then replaced by a **U**-shaped tube containing a few c.cs. of alcoholic silver nitrate, and the heating continued for 15 minutes. If no precipitate forms the operation is finished, but if a precipitate forms, the liquid in the **U**-tube is added to the contents of one of the small flasks and replaced by fresh alcoholic silver nitrate, the heating being continued for another 15 minutes, and so on until no more alkyl iodide passes over.

The contents of the two small flasks are diluted with water, allowed to stand for 5 minutes to ensure decomposition of the last traces of alkyl

iodide, and finally poured gradually into 50 c.cs. of boiling water acidified with nitric acid, which is boiled until the alcohol is driven off. The precipitate is collected in a weighed Gooch crucible, washed, and dried in an air oven at 120°. The percentage is calculated as follows :—

$$\text{Methoxyl} = \frac{\text{wt. of silver iodide}}{\text{wt. of substance}} \times 13{\cdot}21$$

$$\text{Ethoxyl} = \frac{\text{wt. of silver iodide}}{\text{wt. of substance.}} \times 19{\cdot}17$$

*Cumming's Modification.*—(J. S. C. I., 41, 20.)—A convenient apparatus for the estimation of methoxyl groups by the Zeisel method consists of a long-necked round-bottomed flask attached by a ground-glass joint to a bulbed **U**-tube. The methyl iodide generated by the interaction of hydriodic acid and the methoxyl group is absorbed in alcoholic silver nitrate. Pyridine may also be used as absorbent. (J. C. S., 117, 193.) For purification of hydriodic acid, see p. 506.

The apparatus shown in the sketch (Fig. 81) gives very good results.

The flask is of 250 c.cs. capacity, and its neck, from bulb to the ground-glass joint, 25 cms. long. The delivery tube, to which is fixed a side tube, is attached to the flask by means of a ground-glass joint. A thermometer is fixed as shown with its bulb opposite the delivery exit. To the delivery tube is attached also by a ground-glass joint an absorber which contains about 10—15 c.cs. of pyridine. The apparatus is easily filled, emptied and washed.

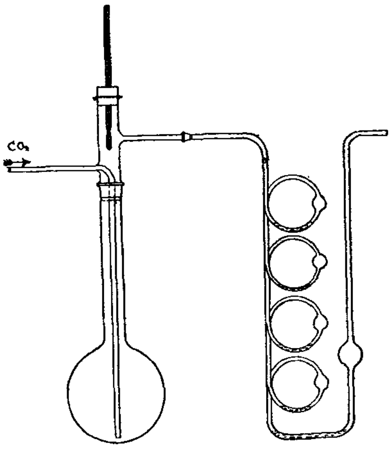



FIG. 81.

When the apparatus is in use, the bulb of the flask containing the hydriodic aid and the substance is heated in an oil bath at 130°. The methyl iodide is carried over into the absorber by a slow current of dry carbon dioxide, passing in at the side tube. The temperature on the thermometer should not be higher than 35°—40° for methoxyl, and 40° for ethoxyl compounds. At these temperatures no hydriodic acid is distilled over. As a further precaution, the neck of the flask is slanted away from the source of heat.

The absorption is complete in about one hour. The pyridine and its methiodide are then washed out with water, acidified with nitric acid, a known volume of silver nitrate added and the excess of the latter estimated by thiocyanate, using ferric alum as indicator.

## Estimation of Esters

1. By hydrolysis with standard alcoholic potash (p. 509). A quantity, 1—2 gms., of the ester is placed in a flask containing 50 c.cs. of semi-normal alcoholic potash. The flask is fitted with a reflux condenser, and the mixture boiled on a water bath for 2—3 hours until hydrolysis is complete. A little water is then run down the inner surface of the condenser into the flask, and the excess of potash in the flask titrated with standard hydrochloric acid, using phenolphthalein as indicator. The quantity of potash used in the hydrolysis gives a measure of the value of the ester.

$$R.COOR_1 + KOH = R.COOK + R_1OH.$$

2. By use of benzene sulphonic acid or phosphoric acid. When the ester yields on hydrolysis products which become coloured in presence of alkali and air, Method 1 is inapplicable. If the acid produced on hydrolysis is volatile in steam, benzene sulphonic or phosphoric acid may be used as hydrolytic agent, and the acid (from the ester) after separation by steam distillation is titrated with standard alkali. (See Estimation of Acetyl Group, p. 479.)

## Estimation of Amides

Amides are estimated by hydrolysis with alkalis (generally aqueous or alcoholic potash) or with acids (sulphuric, phosphoric or benzene sulphonic). In the former case the ammonia set free is absorbed in standard acid (as in the Kjeldahl estimation of nitrogen) and the excess of acid titrated. In the latter the estimation is conducted similarly to a Kjeldahl estimation of nitrogen, the ammonium salt formed on hydrolysis being afterwards decomposed by alkali and the liberated ammonia collected in standard acid.

## Estimation of Aldehydes (other than Formaldehyde)

The method depends on the combination of alkali bisulphites with aldehydes.

25 c.cs. of the solution to be examined, which must not contain more than 0·5% of total aldehyde, are run into 50 c.cs. of a solution of potassium bisulphite containing 12 gms. of $KHSO_3$ per litre, placed in a 150-c.c. flask which is then well corked and allowed to stand for 15 minutes. During this time another 50 c.cs. of the potassium bisulphite solution is titrated with $\frac{N}{10}$ iodine. The excess of bisulphite added to the aldehyde solution is then determined with the same iodine, and from the difference the bisulphite absorbed by the aldehyde, and hence the aldehyde present, can be calculated. The strength given for the bisulphite solution should be adhered to, otherwise the quantities of hydriodic acid liberated in more concentrated solutions reduce the sulphuric acid formed—*i.e.*, the reverse reaction comes into play. The bisulphite method gives an accurate figure also for dilute solutions of mixed aldehydes; combining it with the

cyanide method (see p. 483), the amount of formaldehyde and of another aldehyde in a solution of the two can be estimated.

$$1 \text{ c.c. } \frac{N}{10} \text{ iodine} = 1{\cdot}5 \text{ mgs. } CH_2O$$
$$= 2{\cdot}2 \text{ mgs. } CH_3.CHO$$
$$= \frac{\text{mol. wt. of aldehyde in gms.}}{20} \text{ mgs.}$$

Aldehydes insoluble in water should be dissolved in dilute aqueous alcohol, the concentration of alcohol being kept below 5%.

Aldehydes (*e.g.*, citral, cinnamic aldehyde, etc.) and certain ketones (*e.g.*, acetone) react with hydroxylamine hydrochloride forming oximes with the liberation of hydrochloric acid (Z. a., 1895, 623) which can be titrated in presence of methyl orange.

## Estimation of Formaldehyde

Many methods are available for the estimation of formaldehyde.

1. For pure dilute solutions the following is recommended. 10 c.cs. of the formaldehyde solution which must, if necessary, be diluted so that it is not more than a 2% solution, is mixed with 25 c.cs. of N/10 iodine solution. 10% caustic soda solution, which is free from nitrite, is added, with shaking, drop by drop from a burette until a clear yellow liquid is obtained; after standing for 10 minutes, an equal quantity of 10% hydrochloric acid, *plus* an extra 5 c.cs., are added to liberate the excess of iodine which is back titrated with $\frac{N}{10}$ thiosulphate using freshly made starch paste as indicator.

$$1 \text{ c.c. } \frac{N}{10} \text{ iodine} = 1{\cdot}5 \text{ mg. formaldehyde}$$
$$6NaOH + 3I_2 = NaIO_3 + 5NaI + 3H_2O$$
$$3CH_2O + NaIO_3 = 3CH_2O_2 + NaI$$
$$3CH_2O + 6NaOH + 3I_2 = 3CH_2O_2 + 6NaI + 3H_2O$$
$$CH_2O \equiv I_2 \equiv 2H.$$

The excess of iodine added forms iodide and iodate, and is liberated on addition of hydrochloric acid.

$$5NaI + NaIO_3 + 6HCl = 6NaCl + 3I_2 + 3H_2O.$$

This method is very satisfactory for formaldehyde provided other aldehydes are absent. In a solution containing 1 gm. $CH_2O$ per litre, two titrations should not differ by more than 0·1 c.c. of $\frac{N}{10}$ thiosulphate; and the method will show 1 part of formaldehyde in 100,000 parts of water. It is necessary for such consistency that the quantities of acid and alkali employed be carefully controlled as described; on no account must a great excess of alkali be used, as then there is a danger of some of the formaldehyde being converted to iodoform.

2. For impure dilute solutions of formaldehyde, especially those containing other aldehydes, the cyanide method should be used. The iodine

method is not reliable in this case, as all aldehydes present are attacked. But while aldehydes, other then formaldehyde, combine similarly with potassium cyanide in the cold, they do so slowly ; if the excess of cyanide is removed immediately with silver nitrate, only formaldehyde is estimated. The addition product of formaldehyde and potassium cyanide reduces silver nitrate in the cold. If the silver nitrate solution, however, is acidified with nitric acid before adding the aldehyde-cyanid mixture, no precipitate results if the aldehyde in the latter is in excess. If the cyanide is in excess, 1 mol. of formaldehyde combines with 1 mol. of cyanide, whilst the excess precipitates silver cyanide from the silver nitrate solution.

The details are as follows: 10 c.cs. of $\frac{N}{10}$ silver nitrate acidified with 6 drops of 50% nitric acid are mixed with 10 c.cs. of potassium cyanide solution (prepared by dissolving 3·1 gms. of 96% salt in 500 c.cs. distilled water), the whole diluted to 50 c.cs., well shaken, filtered, and 25 c.cs. of the filtrate titrated with $\frac{N}{10}$ ammonium thiocyanate. Another 10 c.cs. of the potassium cyanide solution, to which 10 c.cs. of the aldehyde solution have just been added, are run in, the whole made up to 50 c.cs., shaken, rapidly filtered, and 25 c.cs. of the filtrate immediately titrated as before. The difference between this and the blank titration gives the amount of potassium cyanide not precipitated by the formaldehyde.

$$1 \text{ c.c. } \frac{N}{10} \text{ thiocyanate} = 3 \text{ mgs. } CH_2O$$

$$CH_2O + KCN = KO.CH_2CN.$$

# CHAPTER XXXIX

## Estimations based on the Use of Titanous Salts

THIS energetic reducing agent can be maintained at constant strength in aqueous hydrochloric acid solution for a reasonable period. It is advisable, however, to re-standardise it after 24 hours' standing. It serves for the reduction of aromatic nitro compounds, some nitroso bodies, many azo dyes, and of nearly all the dyes which yield leuco-compounds. It is easily standardised against a ferric salt—say ferric alum—using potassium thiocyanate as indicator. From the equations :—

$$TiCl_3 + FeCl_3 = TiCl_4 + FeCl_2$$
$$6TiCl_3 + 6HCl + R.NO_2 = 6TiCl_4 + R.NH_2 + 2H_2O$$

it is seen that

$$6TiCl_3 \equiv 6Fe \equiv 6H \equiv NO_2.$$

**Preparation and Storage of Titanous Chloride Solution for Analysis.**—50 c.cs. of the commercial titanous chloride solution (20%) are boiled with 100 c.cs. of conc. hydrochloric acid for 1 minute, and then made up to about 2 litres in a storage bottle A (Fig. 82). The solution when freshly prepared should fill the bottle completely ; otherwise air remains which must be displaced by hydrogen. A is connected to both top and bottom of a burette by means of glass and rubber tubing. The burette has a 2-way glass stopcock at B, so that it can receive solution from A, or deliver solution through its orifice. The second tube from the top of A leads to a hydrogen generator H, which consists of 2 parts, (*a*) an inner tube, made by

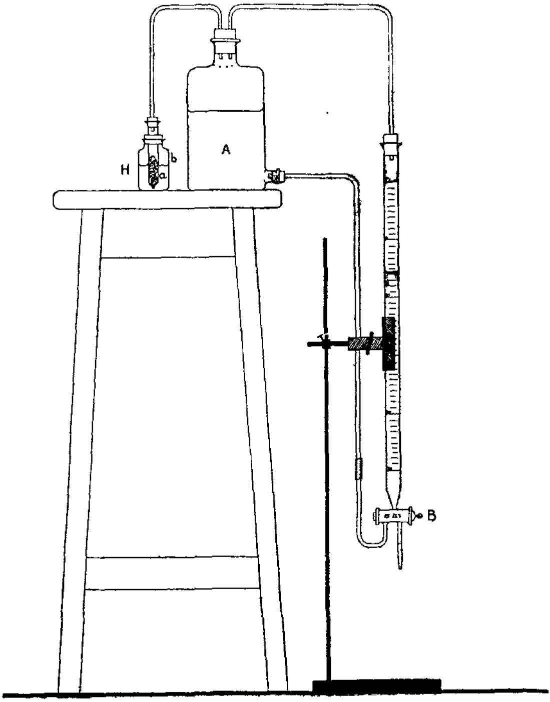



FIG. 82.

drawing a test tube out to a fine point; this contains granulated zinc, and is connected by a rubber stopper and delivery tube to A; (*b*) an outer vessel containing hydrochloric acid (15%). To replace all the air in the apparatus by hydrogen, the stopcock is turned to allow solution from A to fill the tube leading to the bottom of the burette. The stopcock is then turned as for delivery from the burette, and hydrogen allowed to escape from the apparatus for 5 minutes. The burette is filled, emptied and refilled, after which the apparatus is ready for use.

*Standardisation.*—3·5 gms. of pure ferrous ammonium sulphate are dissolved in distilled water, 100 c.cs. of 5N sulphuric acid added, and the whole made up to 250 c.cs. 25 c.cs. of this are oxidised with potassium permanganate solution of approximately $\frac{N}{50}$ strength until a faint pink colour persists. A large excess of potassium thiocyanate (0·2—0·3 gm.) is added, and titanous chloride solution run in from the burette until the red colour due to ferric thiocyanate just disappears. If 25 c.cs. of iron solution require $x$ c.cs. of titanous chloride solution to reduce it, then each c.c. of the latter is equivalent to $\frac{0{\cdot}05}{x}$ gm. iron.

A solution of iron alum, containing about 14 gms. per litre, and acidified with sulphuric acid until the solution assumes a pale straw colour, is prepared. By titrating 25 c.cs. of this with titanous chloride, using potassium thiocyanate as indicator, its strength is determined, and as it will retain its strength for a long period, this alum solution may be used in all subsequent cases for standardising the titanous chloride solution.

Titanous sulphate (p. 503) may be similarly employed. (J. S. C. I., 41, 158.) It has the advantage of not giving rise to halogenated compounds as are given by titanous chloride in some instances.

**Nitro Compounds.**—(*a*) *Those Soluble in Water.*—A known amount of nitro-body is dissolved in water in a conical flask, hydrochloric acid is added, and the solution is boiled with a stream of carbon dioxide passing through. If the nitro compound is volatile in steam the heating should be done in a vessel provided with a "ground in" reflux condenser. (J. S. C. I., 41, 158.) Heating is momentarily stopped, and a large excess of titanous chloride solution run in. The contents are boiled for 10 minutes to ensure complete reduction. Carbon dioxide is passed through the flask during the entire operation. The solution is then cooled and the excess of titanous chloride determined by titration with ferric alum solution, using potassium thiocyanate as indicator. A control experiment without nitro compound present is performed under exactly the same conditions. 6 equivalents of titanous chloride (6 H atoms) are required for the reduction of each $NO_2$ group.

*Example.*—0·4979 gm. *p*-nitroaniline is dissolved in hydrochloric acid on the water bath, and made up to 500 c.cs. 20 c.cs. of this solution are reduced with 50 c.cs. titanous chloride as described above, and the

excess of the latter titrated back with ferric alum. Excess $TiCl_3 = 9{\cdot}7$ c.cs. A control experiment having no *p*-nitroaniline used 0·76 c.c. $TiCl_3$.

$$TiCl_3 \text{ used} = 39{\cdot}54 \text{ c.cs.} \quad 1 \text{ c.c. } TiCl_3 = 0{\cdot}0012228 \text{ gm. Fe.}$$

$$138 \ p\text{-nitroaniline require } 336 \text{ Fe.}$$

$$\therefore 0{\cdot}4979 \text{ gm. contains } \frac{0{\cdot}0012228 \times 39{\cdot}54 \times 138 \times 25}{336} p\text{-nitroaniline}$$

$$= 99{\cdot}7\%.$$

Picric acid and Naphthol Yellow S may be estimated in a similar manner.

(*b*) *Those insoluble in water* must first be sulphonated by heating with 20 parts by weight of fuming sulphuric acid on a water bath for 2 hours. The product is made up to a definite volume with water (*caution!*) and an aliquot part titrated with titanous chloride as described for soluble nitro compounds.

*Example.*—1·01 gms. nitrobenzene are sulphonated as described above, then cooled and the volume carefully diluted to 1 litre. 20 c.cs. are withdrawn and reduced with 50 c.cs. $TiCl_3$ solution (as for *p*-nitroaniline).

$$\text{Excess } TiCl_3 = 18 \text{ c.cs.} \quad \text{Control experiment} = 0{\cdot}8 \text{ c.c. } TiCl_3.$$

$$\text{Vol. } TiCl_3 \text{ used} = 31{\cdot}2 \text{ c.cs.} = 31{\cdot}2 \times 0{\cdot}001700 \text{ gm. Fe.}$$

$$123 \text{ nitrobenzene} = 336 \text{ Fe.}$$

$$\therefore 1{\cdot}002 \text{ gms. contain } \frac{0{\cdot}0017 \times 31{\cdot}2 \times 123 \times 50}{336} = 0{\cdot}9709$$

$$= 96{\cdot}1\%.$$

(*c*) Nitro compounds *insoluble and yet not easily sulphonated*, *e.g.*, dinitrobenzene or dinitronaphthalene, are dissolved in alcohol, and the solution poured into a known volume of titanous chloride solution acidified with hydrochloric acid, through which carbon dioxide is passed. The mixture is boiled, allowed to cool, and the excess of titanous chloride estimated with ferric alum.

*Example.*—0·110 gm. commercial dinitronaphthalene is dissolved in 250 c.cs. alcohol. 50 c.cs. $TiCl_3$ solution are placed in a conical flask, 10 c.cs. conc. HCl added, carbon dioxide passed through, and 25 c.cs. of the dinitronaphthalene solution run in. The mixture is boiled, then allowed to cool, and the excess of $TiCl_3$ titrated.

$$\text{Excess } TiCl_3 = 31{\cdot}60 \text{ c.cs.} \quad \text{Control experiment} = 0{\cdot}90 \text{ c.c. } TiCl_3.$$

$$\text{Vol. } TiCl_3 \text{ used} = 17{\cdot}5 \text{ c.cs.} = 17{\cdot}5 \times 0{\cdot}001750 \text{ Fe.}$$

$$218 \text{ dinitronaphthalene} = 672 \text{ Fe.}$$

$$\therefore 0{\cdot}110 \text{ gm. contains } \frac{0{\cdot}00175 \times 17{\cdot}5 \times 10 \times 218}{672} = 0{\cdot}09933$$

$$= 90{\cdot}3\%.$$

**Nitroso Compounds.**—Owing to the intense colour which these compounds yield in hydrochloric acid solution they may be titrated directly with titanous chloride until the yellow colour disappears. A weighed quantity is dissolved in hydrochloric acid and made up to a known

volume. An aliquot part of this solution is warmed to 40°—50° in a conical flask with carbon dioxide passing through, and titanous chloride solution is run in until the yellow colour disappears. 4 equivalents of titanous chloride are required for each nitroso group.

*Example.*—1·005 gms. nitrosodimethylaniline are dissolved in 20 c.cs. conc. hydrochloric acid and sufficient water to make volume up to 500 c.cs. 10 c.cs. of this solution required 17·5 c.cs. $TiCl_3$ solution.

$$1 \text{ c.c. } TiCl_3 = 0{\cdot}001700 \text{ gm. Fe.}$$
$$150 \text{ nitrosodimethylaniline} = 224 \text{ Fe.}$$
$$\therefore 1{\cdot}005 \text{ gms. contain } \frac{17{\cdot}5 \times 0{\cdot}0017 \times 150 \times 50}{224} = 0{\cdot}9983 \text{ gm.}$$
$$= 99{\cdot}3\%.$$

**Azo Dyes.**—(1) Azo dyes which are soluble in dilute hydrochloric acid may be titrated directly, the disappearance of the colour indicating the end point.

(2) Many azo dyes which are insoluble in dilute hydrochloric acid can be titrated directly in presence of Rochelle salt. Since Rochelle salt forms a compound with titanium, which is pale yellow in dilute solution, this method is inapplicable for the estimation of yellow dyes.

(3) A number of azo dyes which cannot be estimated according to (1) or (2), may be estimated indirectly. A weighed quantity of dye is boiled in aqueous solution in a flask through which a stream of carbon dioxide is passing. After adding hydrochloric acid an excess of titanous chloride is run into the boiling mixture. The reduction is usually complete in about 2 minutes, after which the flask is cooled under the tap with the current of carbon dioxide still passing. When cold, the excess of titanous chloride is estimated with ferric alum solution, using potassium thiocyanate as indicator. The azo group requires 4 equivalents of titanous chloride.

*Example of* (1).—1·003 gms. of Orange II. ($C_{16}H_{11}N_2O_4SNa$) are dissolved in water and made up to 500 c.cs. 50 c.cs. are withdrawn into a conical flask, 5 c.cs. conc. hydrochloric acid added, and after boiling for 1 minute titrated with titanous chloride.

$$\text{Vol. } TiCl_3 \text{ required} = 29{\cdot}15 \text{ c.cs.} = 29{\cdot}15 \times 0{\cdot}00165 \text{ gm. Fe.}$$
$$350 \text{ Orange II.} = 224 \text{ Fe.}$$
$$\therefore 1{\cdot}003 \text{ gms. contain } \frac{29{\cdot}15 \times 0{\cdot}00165 \times 10 \times 350}{224} = 0{\cdot}7522 \text{ gm.}$$
$$= 75\%.$$

*Example of* (2).—1·10 gms. of Diamine Black ($C_{34}H_{24}O_{14}N_6S_4Na_4$) are dissolved in 250 c.cs. water. 50 c.cs. of this solution are withdrawn, 25 c.cs. of Rochelle salt solution (about 20%) added, and titrated with titanous chloride until the colour of the dye disappears.

$$\text{Vol. } TiCl_3 \text{ used} = 20{\cdot}22 \text{ c.cs.} = 20{\cdot}22 \times 0{\cdot}00165 \text{ gm. Fe.}$$
$$960 \text{ diamine black} = 448 \text{ Fe.}$$
$$\therefore 1{\cdot}10 \text{ gms. contain } \frac{20{\cdot}2 \times 0{\cdot}00165 \times 5 \times 960}{448} = 0{\cdot}44 \text{ gm.} = 40\%.$$

*Example of* (3).—0·99 gm. of Chrysophenine G ($C_{30}H_{26}N_4O_8S_2Na_2$) is dissolved in a litre of water. 100 c.cs. of this solution are withdrawn and boiled, with a current of carbon dioxide passing through; 10 c.cs. of conc. hydrochloric acid and 50 c.cs. of titanous chloride are then added, and the mixture boiled until the precipitate dissolves and the solution turns a slight violet colour. After cooling, the excess of titanous chloride is titrated with ferric alum.

$$\text{Excess } TiCl_3 = 34{\cdot}2 \text{ c.cs.}$$
$$\text{Vol. } TiCl_3 \text{ used} = 15{\cdot}8 \text{ c.cs.} = 15{\cdot}8 \times 0{\cdot}00165 \text{ gm. Fe.}$$
$$680 \text{ chrysophenine} = 448 \text{ Fe.}$$
$$\therefore\ 0{\cdot}99 \text{ gm. contains } \frac{15{\cdot}8 \times 0{\cdot}00165 \times 10 \times 680}{448} = 0{\cdot}396 \text{ gm.}$$
$$= 40\%.$$

**Dyes which Yield Colourless Leuco Compounds.**—Approximately 1 gm. is dissolved in 250 c.cs. water; 50 c.cs. of this solution and about 2 c.cs. conc. hydrochloric acid are introduced into a conical flask fitted with a rubber stopper having 3 holes. Through one hole a current of carbon dioxide is introduced, another serves for the escape of this gas, and the third is left for the delivery tube of the titanous chloride burette. The solution is boiled, and then titrated with titanous chloride, until the colour just disappears.

*Example.*—1 gm. crystallised zinc-free Methylene Blue ($C_{16}H_{18}N_3SCl$) is treated as described above. 50 c.cs. of this solution required 41·64 c.cs. titanous chloride solution, of which 1 c.c. = 0·00165 gm. Fe.

$$319{\cdot}5 \text{ Methylene Blue} = 112 \text{ Fe.}$$
$$\therefore\ 1 \text{ gm. contains } \frac{41{\cdot}6 \times 0{\cdot}00165 \times 5 \times 319{\cdot}5}{112} = 0{\cdot}98 \text{ gm.}$$
$$= 98\%.$$

The zinc double chloride of Methylene Blue has the formula $2C_{16}H_{18}N_3.S.Cl, ZnCl_2, H_2O$, and is much less soluble in dilute hydrochloric acid. A drop of weak Methylene Blue solution may be used as indicator in the direct titration of substances with titanous chloride where a selective reduction takes place. The end point is perfectly sharp if the solution is warmed to 35°.

Of other examples which yield leuco compounds, Indigo may be estimated by titrating the sulphonated dye in presence of Rochelle salt; Magenta in Rochelle salt solution; Eosin and Rhodamine in presence of Rochelle salt and alcohol, the latter to keep the leuco compound in solution. All these titrations are carried out on the boiling dye solution and in presence of carbon dioxide.

For many other valuable applications of titanous chloride, see Knecht and Hibbert, "New Reduction Methods in Volumetric Analysis" (Longmans, Green & Co.).

# CHAPTER XL

## ESTIMATIONS BASED ON DIAZOTISATION OR COUPLING

### Preparation of Standard Reagents

(*a*) **Sodium Nitrite.**—Sodium nitrite is often estimated by the use of permanganate and oxalic acid. When impure sodium nitrite is estimated in this manner, the values obtained are often too high, owing to the presence of other oxidisable substances. For reactions such as those which follow, it should be estimated with pure sulphanilic acid, pure benzidine, or pure aniline.

Commercial sulphanilic acid is purified by dissolving in sufficient aqueous sodium carbonate to give an alkaline solution, which is boiled until all trace of aniline disappears. The solution is filtered and acidified with hydrochloric acid, and after 12 hours the product is filtered off and washed with a little water. It is again dissolved by means of hot water and sodium carbonate to a neutral solution; the solution is quickly cooled along with stirring to 0°, and the sodium sulphanilate filtered off. These crystals are dissolved in distilled water, and acidified with pure conc. hydrochloric acid. The crystals which separate are filtered off and washed free of sodium chloride with distilled water; they are once more recrystallised from distilled water, and afterwards dried in an air oven at 120° until of constant weight. The product should be preserved in a bottle having a ground-glass stopper. To prepare a semi-normal solution, exactly 86·5 gms. are dissolved in 50 c.cs. pure (20%) ammonia, and made up to 1 litre; the solution when preserved in the dark will keep for many months.

Benzidine may be purified by crystallisation from boiling water in which it is soluble to about 1%. When crystallised from water above 80° (*i.e.*, from an aqueous solution heated to boiling, cooled to 80° and filtered through a funnel maintained at 80°), the anhydrous base (M.P. 127°) is obtained in meagre quantity; under 80° a hydrate (M.P. 104°—105°) is formed. By crystallisation in the ordinary way, the bulk of the product is the monohydrate. This should be exposed in a desiccator over conc. sulphuric acid until (about 24 hours) a M.P. of 127° is reached. *N.B.*—The melting points must be taken quickly. (J. S. C. I., 46, 209.) The product obtained by vacuum distillation (see Fig. 22) is also suitable for standardisation purposes.

To prepare semi-normal nitrite solution, about 37·5 gms. of commercial sodium nitrite (or rather less of a purer salt) are dissolved in water, filtered, and made up to 1 litre. 50 c.cs. of the $\frac{N}{2}$ sulphanilic acid or $\frac{N}{2}$ benzidine solution are then titrated with it in the following manner:—

The solution is measured by means of a pipette into a 500-c.c. beaker;

200 gms. of ice and 13 gms. of conc. hydrochloric acid are also added. The beaker is slightly tilted to one side, and the nitrite solution, run in from a burette, is allowed to trickle down the side of the beaker and thus to sink quickly to the bottom. When about 45 c.cs. nitrite have been added, the solution is stirred with a glass rod, and more nitrite is run in, drop by drop (tests being carried out at intervals), until a drop of the solution just causes an immediate blue coloration on starch-iodide paper.* After standing a few minutes, a test is again applied to see if the excess of nitrite still remains, and if not, more nitrite is added, until a slight positive test is obtained after a few minutes' standing. It is advisable to repeat the operation, all but 1 c.c. of the total volume of nitrite used in the previous test being run in at once along the side of the beaker; this obviates as much as possible the escape of free nitrous acid on mixing. The remainder of the nitrite is run in, drop by drop, as before. From the volume of nitrite necessary, a calculation is made to ascertain what volume of water must be added to make the remaining nitrite exactly semi-normal.

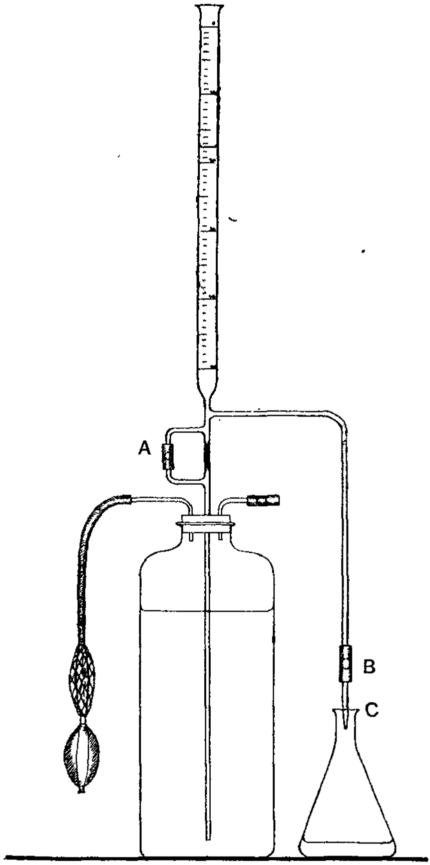


FIG. 83.

Fig. 83 shows a convenient type of burette for use in cases where many titrations have to be performed. The burette is fixed to the storage bottle and the liquid is blown up into the burette by compressed air from the hand bulb, the bead at A being opened by pressure between the fingers. The titration is effected by opening the bead at B.

(*b*) $\frac{N}{2}$ **Aniline Solution.**—About 250 c.cs. of the purest commercial

* A certain amount of practice is necessary to judge the end point accurately, as the paper when moistened with diazonium solution generally develops a blue colour on standing a short time. As the end point is approached the eye detects a brief interval between the moistening of the test paper and the development of the colour; at the end point this interval disappears and the colour develops instantaneously. (See p. 504.)

aniline are carefully redistilled, and the fraction passing over within half a degree at its boiling point reserved for the preparation of the standard solution. Exactly 46·5 gms. of the above fraction are weighed; to this are added 50 c.cs. ice-water, and 75 c.cs. of conc. hydrochloric acid, the object of the ice-water being to prevent the escape of fumes when the acid and amine come together. The solution is then made up to 1 litre with distilled water; when prepared in this way, it is generally accepted as exactly semi-normal, and may be used as such for the standardisation of sodium nitrite solution; however, if any doubt exists, it is standardised against the previously prepared $\frac{N}{2}$ sodium nitrite.

(*c*) $\frac{N}{20}$ **Phenyldiazonium Solution.**—50 c.cs. of the $\frac{N}{2}$ aniline solution are measured out into a 500-c.c. flask, 10 c.cs. of conc. hydrochloric acid are added, and the flask immersed in ice-water. When thoroughly cold, 50 c.cs. of $\frac{N}{2}$ sodium nitrite are run in from a burette, the contents of the flask being gently rotated at intervals. After standing for 15 minutes, the solution is made up to 500 c.cs.; it may be preserved for a few hours at 0° in the dark, but should always be freshly prepared before use.

(*d*) $\frac{N}{20}$ **R Salt Solution.**—20 gms. of commercial "R Salt" (β-naphthol-3 : 6-disodium-disulphonate) are dissolved in water and made up to 1 litre to give an approximately $\frac{N}{20}$ solution. A $\frac{N}{20}$ phenyldiazonium solution is prepared and 100 c.cs. of it poured into a 100-c.c. measuring cylinder which has been previously cooled in an ice chest. The cylinder is then immersed in a vessel containing ice-water. 50 c.cs. of the R salt solution are measured out into a beaker, 8 gms. sodium carbonate added, and stirred to dissolve. 15 c.cs. of the phenyldiazonium solution are then added from the measuring cylinder. A red dye is formed which is thrown out of solution by addition of common salt. After addition of sufficient salt, a drop "spotted" on filter paper leaves a sediment of dye in the centre, and the outspread is colourless. A small quantity of diazonium solution from the stock solution is poured into a small beaker to be used for testing. If the outspread on filter paper of a drop from the solution containing the dye is touched with a glass rod dipped in the diazonium test solution, a red dye is formed, provided an equivalent quantity or more of diazonium solution has not been added. Proceeding in this way, and testing after each addition, small quantities of diazonium solution from the measuring cylinder are added until a drop tested on filter paper no longer forms a red dye.

When the dyestuff is very soluble in water, a clear outcrop can frequently be secured by the following procedure. The coloured solution is "spotted" on to a small heap of common salt placed on good filter paper and allowed to soak through to the paper. The salt may then be

removed by shaking the paper, and the test applied to the clear outcrop as before.

Since 1 mol. of R salt couples with 1 mol. of diazonium compound, the strength of the R salt solution can be easily calculated, and hence the quantity of water which must be added to make it $\frac{N}{20}$.

Standard " R salt " is used for estimating amines (see below).

### Estimation of Amines

(*a*) *By Diazotisation.*—Many amines which diazotise readily can be accurately estimated with standard nitrite. The principle of the method is exactly the same as that underlying the standardisation of sodium nitrite with sulphanilic acid, benzidine or aniline. As a general rule 1/100 mol. wt. of the amine is dissolved along with rather more than three times its acid equivalent of hydrochloric acid in water; the solution is cooled to 0° by the addition of ice, and $\frac{N}{2}$ sodium nitrite solution is run in until an end point is indicated by starch-iodide paper (see preparation of standard sodium nitrite, p. 490).

$$\% \text{ purity} = \text{c.cs. of } \frac{N}{2} \text{ nitrite} \times 5.$$

Those amines which, when treated as above, give diazoamino compounds or dyes and also those whose diazonium compounds blacken starch-iodide cannot be estimated directly. They may be estimated either by (1) coupling with a standard diazonium solution, or (2) by adding excess of nitrous acid and coupling with alkaline $\beta$-naphthol of known strength.

(*b*) *By Diazotisation and Coupling.*—Exactly $\frac{1}{100}$ mol. wt. of the amine is diazotised as described under (*a*). 8 gms. sodium carbonate are added to the diazotised solution and stirred until dissolved. The solution is diluted and cooled, so that its strength is equivalent to about 1% amine and its temperature about 5°. $\frac{N}{20}$ R salt solution is then run in until an excess of diazonium solution no longer appears on spotting on paper (see p. 492), the dye being first salted out by the addition of common salt. By the above method, two values are obtained—a " nitrite " value, and an " R salt " value, and these should approximate.

The above outline is general, but is subject to variation for the particular amine under estimation. For instance, the amount of sodium carbonate—the essential point is to have the mixture alkaline during the coupling—depends on the acidity of the diazonium solution, and the presence of acid groups, such as sulphonic. When the coupling is carried out in acetic acid solution, sodium acetate is added in place of sodium carbonate and in three times the quantity.

### Estimation of Phenolic Compounds

Phenolic compounds which couple readily and completely with diazonium compounds can be estimated by titration with a standard diazonium solution. The standardisation of R salt affords one example of the method.

*Example.*—**β-Naphthol.**—1·44 gms. ($\frac{1}{100}$ mol.) of β-naphthol are dissolved in 10 c.cs. caustic soda solution (15%); to this is added 100 c.cs. water and 3 gms. of anhydrous sodium carbonate. The whole is then made up to 200 c.cs. in a flask. 50 c.cs. of this are placed in a beaker, and ice-cold $\frac{N}{20}$ phenyl-diazonium solution run in until a drop on filter paper no longer shows an excess of β-naphthol when tested with diazonium solution. (For end point see R salt, p. 492.)

$$\% \text{ purity} = \text{c.cs. of diazonium solution} \times 2.$$

### Estimation of H Acid (Acid Sodium Salt)

(*a*) *By Diazotisation.*—3·41 gms. ($\frac{1}{100}$ mol.) are dissolved in 5 c.cs. of 10% sodium carbonate solution and diluted to 250 c.cs. 25 c.cs. of conc. hydrochloric acid are then added, and the solution diazotised at 5° with $\frac{N}{2}$ sodium nitrite.

$$\% \text{ of H acid} = \text{c.cs. of nitrite} \times 5.$$

(*b*) *By Coupling.*—3·41 gms. H acid are dissolved in 50 c.cs. of 10% sodium carbonate and diluted to 300 c.cs. $\frac{N}{20}$ phenyldiazonium solution is then added until the end point is obtained as determined by "spotting" (see p. 492).

$$\% \text{ of H acid} = \frac{\text{c.cs. of diazonium solution}}{2}.$$

For a good quality of H acid, the percentage determined by diazotisation should only be slightly higher than that determined by coupling.

# CHAPTER XLI

## MISCELLANEOUS ESTIMATIONS

### Estimation of *p*-Phenylenediamine

THE *para*-diamines cannot be estimated by means of the diazo reaction. The following estimation is based on the formation of benzoquinone dichloro-imide when *p*-phenylenediamine in hydrochloric acid solution is added to a solution containing excess of sodium hypochlorite and sodium carbonate.

A solution of sodium hypochlorite is prepared by diluting 50 c.cs. of a commercial solution containing about 12—15% available chlorine to 1,000 c.cs. Or, a corresponding solution may be prepared by passing chlorine into caustic soda (p. 512). 50 c.cs. of this solution are titrated with $\frac{N}{10}$ sodium arsenite solution, using starch-iodide paper as indicator. 100 c.cs. of hypochlorite solution are then measured out, diluted with an equal volume of cold water, and about 1 gm. of solid sodium carbonate added. 10 c.cs. of the solution to be determined, containing 2—6% of *p*-phenylenediamine dissolved in slight excess of hydrochloric acid, are added slowly with stirring. The mixture should then give a strong reaction with starch-iodide paper, otherwise the experiment must be repeated, using either less diamine or more sodium hypochlorite solution. On the addition of the diamine solution, the dichloro-imide is rapidly precipitated as an almost colourless solid.

$$C_6H_4(NH_2)_2 + 3Cl_2 \longrightarrow C_6H_4 : (NCl)_2 + 4HCl.$$

The turbid solution is then titrated, without filtration, with $\frac{N}{10}$ sodium arsenite solution, using starch-iodide paper as external indicator, the end point being sharply defined by the disappearance of the blue colour on spotting. At the end of the titration the solution should be alkaline, because the dichloro-imide in alkaline solution has no action on the test-paper. The difference in the volume of the $\frac{N}{10}$ arsenite solution required for the titration of the sodium hypochlorite itself and for the titration of the hypochlorite *plus* diamine is equivalent to the amount of active chlorine removed from the solution as benzoquinone dichloro-imide, each c.c. of $\frac{N}{10}$ arsenite solution corresponding to 0·0018 gm. of diamine.

The method gives good results, the error varying from 0·3—0·7%. (J. S. C. I., 38, 408.)

## Estimation of Thiophen in Benzene

2 c.cs. of commercial benzene and 20 c.cs. of Denigès' reagent (see below) are introduced into a strong test tube (2 cms. × 15 cms.), which is afterwards closed with a good wet cork, and placed in a shaking machine for 3 hours. (Even without shaking, the reaction takes place to some extent.) At the end of this time, the precipitate is collected in a weighed Gooch crucible, washed with hot water until neutral to litmus, dried at 110°—115° until constant, and weighed as $2(HgO.HgSO_4)C_4H_4S$. The weight of this precipitate × 0·0757 gives the weight of thiophen.

To prepare the above reagent, 20 c.cs. of pure conc. sulphuric acid are poured into 110 c.cs. distilled water, 5 gms. of finely powdered mercuric oxide are added and the mixture stirred until almost all dissolves. The solution is then filtered and the filtrate preserved in a stoppered bottle.

The Gooch crucible is prepared with a filtering layer of good fibrous asbestos on top of which is placed a perforated porcelain plate. The asbestos should be previously purified by boiling first with *aqua regia* for a short time, and then with conc. hydrochloric acid for a week, the acid being renewed each day. (J. S. C. I., 38, 189.)

## Estimation of Enol Modification in a Compound exhibiting Keto-enol Tautomerism

The enolic form reacts instantly with an alcoholic solution of bromine, and the amount of bromine used corresponds with the formation of a dibromide, which body, however, cannot be isolated since it decomposes as soon as formed into hydrogen bromide and a bromo-ketone.

$$\begin{array}{l} —COH \\ \quad \| \\ —CH \end{array} \rightarrow \begin{array}{l} —C(Br)OH \\ \quad | \\ —CHBr \end{array} \rightarrow \begin{array}{l} —C{:}O \\ \quad | \\ —CHBr \end{array} + HBr.$$

The amount of enolic compound can be estimated by adding a standard solution of bromine in alcohol, until the yellow colour just persists, but the method has the disadvantage that such a solution of bromine is unstable.

In the following method a slight excess of an alcoholic solution of bromine is added to an alcoholic solution of the tautomeric mixture; the excess of bromine is immediately removed by the addition of a few drops of alcoholic $\beta$-naphthol solution; potassium iodide solution is next added, and the hydrogen iodide formed by interaction with the hydrogen bromide present reduces the bromo-ketone with liberation of free iodine, which is estimated by titration with standard thiosulphate (in absence of starch). One molecule of iodine ≡ one molecule of enolic compound. For criticism of this method, see Ann. Rep., 1930, 100.

$$\begin{array}{l} —CO \\ \quad | \\ —CHBr \end{array} \xrightarrow{2HI} \begin{array}{l} —CO \\ \quad | \\ —CH_2 \end{array} + I_2 + HBr.$$

*Example.*—**Ethyl Acetoacetate.**—The following reagents are prepared :—

1. An approximately $\frac{N}{10}$ alcoholic bromine solution ; the bromine itself being previously purified by shaking up with sulphuric acid, then separating and distilling.
2. A 10% solution of potassium iodide.
3. $\frac{N}{10}$ sodium thiosulphate solution.
4. 1 gm. of $\beta$-naphthol dissolved in 20 c.cs. alcohol.

1·625 gms. ester are dissolved in 100 c.cs. alcohol in a flask, and cooled to −7°. The contents are given a swirling motion, and ice-cold bromine solution (21 c.cs.) added until a faint yellow colour is produced. Alcoholic $\beta$-naphthol sufficient to remove colour is then added. The time for the addition of bromine and $\beta$-naphthol should not exceed 20 seconds. 5 c.cs. of the potassium iodide solution are added, and the contents titrated with $\frac{N}{10}$ thiosulphate. Volume of thiosulphate = 18·7 c.cs., which is equivalent to 18·7 × 0·0127 gm. iodine, or to 18·7 × 0·0065 gm. enolic ester.

$$\therefore \% \text{ Enol} = \frac{100 \times 18{\cdot}7 \times 0{\cdot}0065}{1{\cdot}625} = 7{\cdot}49.$$

## Estimation of Anthracene in Commercial Anthracene

The estimation of anthracene depends on its oxidation by means of chromic acid to anthraquinone.

1 gm. of the sample is dissolved in 45 gms. of glacial acetic acid by heating on a sand bath under a long reflux condenser. When the contents of the flask are boiling, 15 gms. of crystallised chromic acid dissolved in 50% acetic acid are very gradually added (2 hours). When the addition of chromic acid is complete, the mixture is boiled for another 2 hours. After cooling, the contents are treated with 400 c.cs. water, and the precipitated anthraquinone filtered off, washed with cold water, then with boiling dilute alkali and finally with boiling water, until the washings are free from alkali. The residue is then washed into a small porcelain basin and dried at 100°. 10 gms. of Nordhausen sulphuric acid (about 5% $SO_3$) are added, and the mixture heated for 10 minutes at 100°. After cooling, it is carefully poured (*caution !*) into 200 c.cs. of cold water, the anthraquinone filtered, washed with dilute alkali, and finally with water as before. It is then dried and weighed. The anthraquinone is volatilised by heating on a sand bath and the residue is weighed. The difference gives the weight of anthraquinone.

$$\text{Wt. of anthraquinone} \times \frac{178}{208} = \text{weight of anthracene.}$$

## Estimation of Acetone

1. *Volumetrically.*—Iodine in alkaline solution reacts with acetone to give iodoform, a reaction which is used in the estimation of the ketone.

$$1 \text{ mol. acetone} \equiv 3 \text{ mols. iodine.}$$

$$CH_3COCH_3 + 3KIO \rightarrow CH_3COCI_3 + 3KOH$$
$$CH_3COCI_3 + KOH \rightarrow CHI_3 + CH_3COOK.$$

The excess of iodine may be decomposed as follows :—

$$I_2 + 2KOH = KIO + KI + H_2O$$
$$KIO + KI + 2HCl = I_2 + 2KCl + H_2O$$

and is titrated with thiosulphate solution.

A weighed quantity (about 2 c.cs.) of acetone is made up to 500 c.cs. with water. 15 c.cs. of this solution are shaken with 50 c.cs. of approximately normal caustic potash in a 250-c.c. stoppered flask. About 100 c.cs. of $\frac{N}{10}$ iodine solution are then run in from a burette, and the mixture shaken for ten minutes. It is then acidified with about 50 c.cs. of approximately normal sulphuric acid. The excess of iodine which is thereby liberated is titrated with $\frac{N}{10}$ thiosulphate ; this amount deducted from the quantity of iodine originally added gives the amount of iodine used.

$$1 \text{ c.c. of } \frac{N}{10} \text{ iodine} \equiv 0{\cdot}000968 \text{ gm. acetone.}$$

*Example.*—

| | | |
|---|---|---|
| | Weight of acetone | = 2·0 gms. |
| | Volume of acetone solution | = 15 c.cs. |
| „ | $\frac{N}{10}$ iodine added | = 82·5 c.cs. |
| „ | $\frac{N}{10}$ thiosulphate | = 21·0 c.cs. |
| ∴ „ | $\frac{N}{10}$ iodine used up | = 61·5 c.cs. |

$$\therefore \text{ Wt. of acetone in 15 c.cs. solution} = 61{\cdot}5 \times 0{\cdot}000968 \text{ gm.}$$

$$\text{,, \quad ,, \quad 500 c.cs. solution} = \frac{61{\cdot}5 \times 0{\cdot}000968 \times 500}{15} \text{ gms.}$$

$$\therefore \% \text{ Acetone} = \frac{61{\cdot}5 \times 0{\cdot}000968 \times 500 \times 10}{15 \times 2}$$

$$= 99{\cdot}38.$$

2. *Gravimetrically.*—Mercuric sulphate combines with aliphatic ketones to give insoluble precipitates which, when dried *in vacuo*, have the general formula $(2HgSO_4.3HgO).4COR_2$. These compounds have such high molecular weights that very small quantities of the ketone suffice.

5 gms. of mercuric oxide are dissolved in 120 c.cs. of cold 30% sulphuric acid. 25 c.cs. of this solution and 25 c.cs. of the acetone solution, containing about 0·05 gm. of acetone, are placed in a strong glass bottle of about 200 c.cs. capacity. The glass stopper is wired in, and the bottle heated to 100° on a water bath for 10 minutes. When cold, the whole is filtered through a weighed filter paper, and the residue washed with cold water, dried *in vacuo* for 12 hours and weighed.

Wt. of acetone = weight of precipitate × 0·0584.

*Example.*—

| | | |
|---|---|---|
| | Wt. of acetone in 25 c.cs. of water | = 0·052 gm. |
| | ,, precipitate | = 0·886 ,, |
| ∴ | ,, acetone | = 0·886 × 0·0584 |
| | | = 0·0517 gm. |

$$\therefore \ \% \text{ acetone} = \frac{0{\cdot}0517 \times 100}{0{\cdot}052} = 99{\cdot}4$$

See also p. 482 (Oxime method).

## Estimation of Glucose or Cane Sugar in Solution by means of Fehling's Solution

*Fehling's Solution* consists of two parts. The first, a solution of 69·28 gms. of pure crystalline copper sulphate dissolved in water with the addition of 1 c.c. of pure sulphuric acid, and the whole made up to 1 litre; the second, a solution of 350 gms. of Rochelle salt (sodium potassium tartrate) and 120 gms. of sodium hydroxide (purified from alcohol) dissolved in water and made up to 1 litre. Equal volumes of these two parts are mixed just before use. Each c.c. of the resulting solution is equivalent to 0·005 gm. glucose or to 0·00475 gm. cane sugar. The solution deteriorates after a time, and should be standardised frequently against pure glucose or pure cane sugar.

*Standardisation.*—Some pure glucose is dried for 12 hours in a vacuum desiccator over sulphuric acid and a solution of known concentration (0·5—1%) made.

5 c.cs. of each part of the Fehling's solution are measured out into a porcelain dish, diluted with 40 c.cs. of dilute caustic soda solution, and gently boiled. Glucose solution, about 1 c.c. at a time, is then run from a burette, and the mixture boiled after each addition until the blue colour is finally discharged.

The titration is then repeated, all but 2 c.cs. of the volume of glucose solution used in the first determination being run in at once, and the remainder in drops until the blue colour just vanishes. The end point is more easily observed when the dish is slightly tilted. Several determinations are made until concordant results are obtained. If the end point is indistinct, a dilute acetic acid solution of potassium ferrocyanide "spotted" on a white plate may be used as external indicator. A brown coloration is observed so long as copper is present in solution.

Alternatively the standardisation may be carried out with a solution of "invert sugar" prepared by heating 4·75 gms. of cane sugar with 50 c.cs. of 2% hydrochloric acid to boiling for 10 to 15 minutes, then cooling, neutralising exactly with sodium carbonate, and diluting to 1 litre.

*Estimation of Glucose or Cane Sugar in Solution.*—The estimation of glucose or "inverted" cane sugar solution is carried out similarly to the foregoing standardisations. The concentration must be of the order of 0·5—1%, otherwise reliable results are not obtained. As cane sugar does not reduce Fehling's solution until inverted, a mixture of cane sugar and glucose may be estimated by determining the glucose prior to inversion, and then the total glucose and fructose after inversion. Fructose, galactose, mannose, maltose, lactose, may be estimated similarly, but the results are not satisfactory in all cases.

Instead of measuring the volume of the Fehling's solution, the hot solution of sugar may be mixed with an excess of Fehling's solution, heated in a boiling water bath for 15 minutes, and the precipitated cuprous oxide estimated in either of the following ways :—

1. By filtration through a weighed "asbestos" Gooch crucible, washing first with hot water, then with alcohol, and finally with ether, and drying for 30 minutes in a steam oven.

2. By filtration (as in 1.), washing with hot water, then dissolving the $\mathbf{Cu_2O}$ in a known volume of $\frac{N}{5}$ permanganate solution previously diluted with 4 times its volume of 25% sulphuric acid, and titrating the excess of permanganate at 40°—50° with an $\frac{N}{5}$ solution of oxalic acid. 1 c.c. of $\frac{N}{5}$ permanganate is equivalent to 0·01426 gm. cuprous oxide, or to 0·01426 × 0·5045 gm. glucose or to 0·01426 × 0·4793 gm. cane sugar. (J. S. C. I., 16, 981.)

## Estimations using Potassium Bromate

The method depends on the direct bromination of a substance by means of nascent bromine liberated from potassium bromate and potassium bromide in hydrochloric acid solution.

$$5KBr + KBrO_3 + 6HCl = 6KCl + 6Br + 6H_2O.$$

The corresponding sodium salts, which are cheaper, serve equally well. Excess of potassium bromide and hydrochloric acid is added to a solution of the substance to be estimated ; and the bromate, in the form of a volumetric solution (usually N/5), is run in. The end point (shown by the presence of free bromine) is detectable, quite sharply, by spotting on starch-iodide paper as external indicator. Alternatively the end point may be determined by adding a known amount of bromate in excess, then potassium iodide, and titrating the liberated iodine with thiosulphate.

*Preparation of N/5 Bromate Solution.*—5·567 gms. (1/30 mol.) of potassium bromate are dissolved in water to 1,000 c.cs. 25 c.cs. are withdrawn, diluted to 200 c.cs. with water, 3—5 gms. of potassium bromide (free from bromate), 3—5 gms. potassium iodide (free from iodate) and 5 c.cs. conc. hydrochloric acid (free from chlorine or iron) added. The liberated iodine is titrated with thiosulphate in the usual way, and the bromine equivalent of the bromate solution thus obtained.

The reagent is particularly suitable for the determination of amines and phenols and their derivatives, and also for unsaturated compounds. Temperature has a marked effect on the rate and on the extent of bromination. It is necessary to know or to determine what bromo compound is being formed.

In the case of amines and phenols, bromine enters the ring in the ortho- or para- position; if there is no unoccupied ortho- or para-position bromination does not take place except when this position is occupied by a carboxyl or sulphonic group, and in such case the group is split off and replaced by bromine.

*General Procedure.*—Dissolve 0·2—0·5 gm. of the compound to be estimated in 200 c.cs. of water, using a slight excess of hydrochloric acid for amines or a similar excess of caustic soda in the case of phenols, carboxylic- and sulphonic-acids. To the solution thus prepared 10 c.cs. of a 20% solution of potassium bromide and 5—10 c.cs. of concentrated hydrochloric acid are added; the mixture is brought to the required temperature and N/5 bromate solution run in slowly until a sample withdrawn gives a reaction on starch-iodide paper. The presence of free bromine should be again tested for after 5 minutes.

*Examples.*—Aniline is rapidly tribrominated at room temperature, the end point is very sharp, and this estimation of aniline is preferable to the nitrous acid method. At ordinary temperature ortho- and para-toluidines are dibrominated and meta-toluidine is tribrominated. Dimethylaniline is monobrominated at 0°—5°, dibrominated at 40°—50° and tribrominated at 60°—70°, an interesting example of the effect of temperature. Sulphanilic acid at 60°—70° yields tribromoaniline, and at this temperature *p*-nitroaniline reacts quantitatively. Phenol at about 22° yields tribromophenol. For reference to the estimation of *m*-diamines, *m*-dihydroxy compounds, R salt, cresols, *p*-nitroaniline, diphenylamine, *p*-nitrophenol, and other notes, see J. S. C. I., 41, 161.

## Estimation of Formic Acid

This acid can be estimated by reduction of mercuric chloride (*a*) volumetrically (Abs., 1875, 1051), (*b*) gravimetrically (Abs., 1923, 95), or by reduction of potassium permanganate (Abs., 1906, 907). In presence of homologues it can be estimated by the method given in Abs., 1912, 499, the total acidity being determined by titration with alkali and the formic acid by reduction of permanganate.

# PART IV

## CHAPTER XLII

### INORGANIC SECTION

### Reagents

**Sulphuric Acid.**—The acid used in the laboratory is the commercial 96—98% acid. The 100% acid (monohydrate) can be made from this by adding the requisite amount of oleum (see p. 314). Usual impurities: lead sulphate and oxides of nitrogen.

**Oleum.**—Oleum is supplied in all strengths up to 70% free $SO_3$. From 0—40% free $SO_3$ it is liquid; from 40—60% free $SO_3$ it is solid; from 60—70% free $SO_3$ it is liquid; above 70% it is solid. The acid should be kept in well-stoppered, stout glass bottles, and when it is necessary to melt the acid, the stopper is withdrawn, a watch-glass placed on the mouth of the bottle, and the bottle placed on a layer of sand in a large vessel or oil bath which is warmed with a small flame. The bottle is fitted with a wash-bottle attachment, and any desired quantity is forced out by gentle air pressure from hand or foot bellows (the mouth must not be used). For the preparation of oleum of definite strengths, see p. 314. Usual impurities: ferric sulphate, sulphur dioxide and lead sulphate. For estimation, see p. 313.

**Hydrochloric Acid.**—The pure concentrated aqueous acid contains about 33% $HCl$. The commercial acid containing about 30% $HCl$ serves for most organic preparations. The yellow colour is due to iron. Usual impurities: chlorine, sulphuric acid and iron.

**Hydriodic Acid.**—Both the conc. acid and the acid of constant boiling point (D. 1·7, 57% $HI$ (see p. 506) ) are on the market. Usual impurity: iodine.

**Nitric Acid.**—The commercial conc. acid generally contains about 70% $HNO_3$. Fuming nitric acid (see p. 512) containing about 95% $HNO_3$ (D. 1·5) is available commercially. Usual impurities: oxides of nitrogen, sulphuric acid, hydrochloric acid, chlorine and iodine.

**Phosphoric Acid.**—The commercial acid (D. 1·5) contains 65% $H_3PO_4$; syrupy phosphoric acid contains about 90% $H_3PO_4$. Usual impurities: sulphuric acid, iron and arsenic acid.

**Anhydrous Aluminium Chloride.**—It is best to buy this reagent from a reliable manufacturer. As a high pressure frequently exists in bottles containing this reagent, such bottles should be opened with care, a cloth being wrapped round the vessel during the operation. If the commercial product is not available, it may be prepared (see p. 506). Contains

adsorbed hydrogen chloride up to 9 c.cs. per gm. (C. J. R., 1, 400); absorbs moisture very readily.

**Titanous chloride** comes on the market in the form of a 20% solution (see p. 485). Usual impurities: oxidation products. For the many reducing reactions in which titanous chloride is used it may be replaced by titanous sulphate (obtainable as 20% solution), which should be used when there is possibility of chlorination.

**Copper Bronze** (Kahlbaum, "Natur Kupfer").—This product can be used for the Gattermann reaction (p. 155) in place of copper powder (p. 508). The bronze should be washed with ether to remove oil and grease.

**Zinc Dust.**—Commercial varieties vary much in character and are subject to deterioration; they contain usually 90—95% **Zn** (for estimation, see p. 510); they should be preserved in airtight vessels and should be occasionally estimated. Two other forms of zinc for reducing purposes are on the market—a ground zinc, made by grinding metallic zinc, and a variety in the form of powder containing 2% of lead, which gives specially good results. Usual impurities: zinc oxide, iron and arsenic.

**Caustic Soda.**—This is supplied in powder, stick, flake and pellet forms, the last two being convenient to use. The pure variety comes on the market in the form of sticks. In weighing out a quantity, the sticks should not be handled. Pieces of a desired size can be broken off by elevating one end and dealing a sharp blow with a knife or file at the desired point. The same remark applies to caustic potash sticks. 30—40% solutions of caustic soda are available in commerce. Usual impurities: chloride, carbonate, and chlorate of sodium.

**Ammonia.**—A solution, D. 0·88, containing 35% $NH_3$ comes on the market. Cylinders of anhydrous liquid ammonia are also available.

**Sodium Nitrite.**—The commercial product contains 97—98% $NaNO_2$, and is suitable for most organic reactions. For estimation, see p. 490. Usual impurity: sodium nitrate.

**Sodium Sulphide ($Na_2S$, $9H_2O$).**—The commercial variety consists of deliquescent crystals. It can be used for most purposes. Usual impurities: polysulphides and sulphate. For estimation, see p. 512.

**Sodium Bisulphite** (see p. 510).—This is available commercially in the solid form, and as a 30% solution. The product as prepared on p. 510 is the most reactive in many cases. Usual impurity: bisulphate.

**Sodium Hypochlorite** (see p. 512).—The commercial solution (about 15%) is available. Usual impurities: caustic soda, sodium chloride and sodium chlorate.

**Iron Filings and Iron Powder.**—These are recommended for many operations in place of zinc and tin, on account of cheapness. Usual impurities: oxides.

**Stannous Chloride.**—The product should be obtained from a reliable firm. It should be frequently estimated, as it deteriorates through oxidation (see p 513).

Tables of the gravities and strengths of some reagents are given on pp. 514, 515.

## Indicators

1. **Litmus Paper.**—Used as an indicator for all weak and strong acids and bases. Turned red by acids and blue by alkalis.

Cubes of best quality litmus containing 50—90% calcium sulphate are ground and washed with benzene, then with alcohol. 4—5 gms. of the residue are then dissolved in 1 litre of water ; good quality filter paper is soaked in the solution and dried by hanging on threads. It is then cut into small pieces.

For red litmus a few drops of acetic acid are added to the solution, and for blue litmus, ammonia is used.

2. **Phenolphthalein Paper.**—Used in acidimetry and alkalimetry. Turned red by alkalis, reacting with ammonia and sodium carbonate, but not with bicarbonate. Used chiefly in analytical work.

0·5 gm. of phenolphthalein is dissolved in 500 c.cs. of hot water, and filter paper is soaked in the hot solution and dried.

A few drops of a very dilute alcoholic solution may be used as an internal indicator.

3. **Congo Paper.**—Used as an indicator for acids. Turned pure blue by mineral acids and violet by strong organic acids.

1 gm. Congo Red is dissolved in 1 litre of water to which a few drops of ammonia have been added. Filter paper is soaked in the warm solution and dried.

4. **Brilliant Yellow Paper.**—Used as an indicator for alkalis. Turned red by alkalis and by alkali carbonates and ammonia.

1 gm. of the dye is dissolved in 1 litre of water and filter paper dipped in the solution and dried.

The alkali salts of phenols and naphthols also give an alkaline reaction, so that free alkali must be tested for in the following way. A crystal of ammonium chloride is added to a few drops of the solution placed on a watch-glass, and the latter warmed with a very small flame. Another watch-glass with a piece of moistened red litmus paper adhering to its concave side is placed over the other one, and if the liquid is alkaline the litmus paper will be turned blue. This method can also be used where the colour or solubility of the substance to be tested prohibits the direct use of test papers.

5. **Thiazole Paper (Mimosa Paper).**—Used as an indicator for free alkali and is preferable to turmeric. Turned red by alkalis, but not influenced by ammonia even in high concentrations.

Prepared similar to Congo Red paper, the dye thiazole yellow (Clayton Yellow) being employed.

6. **Starch-Iodide Paper.**—Used as an indicator for nitrous acid, and for halogens and other oxidising agents. Turned bluish-violet by a trace of oxidising agent and brown by excess.

10 gms. of pure starch are ground up with 100 c.cs. of cold water and

the mixture poured slowly into 2 litres of boiling water with good stirring. The whole is boiled for a few minutes, then cooled rapidly. 2 gms. of potassium iodide are added and 1 gm. of cadmium iodide. When all is dissolved, filter paper is immersed, drained, and dried in an atmosphere free from fumes.

The solution does not keep and should be freshly prepared.

The solution may be used as an indicator by "spotting" on filter paper.

When the paper is used, a drop of the test solution is removed on a glass rod, and *lightly* drawn across the paper.

The papers should be tested from time to time by treating with a 1% solution of hydrochloric acid containing 1 drop of very dilute sodium nitrite solution.

7. **Lead Acetate Paper.**—Used for detecting $\mathbf{H_2S}$, with which it gives a brown coloration. Filter paper is soaked in a solution of 5 gms. lead acetate (or nitrate) per litre, and dried in an atmosphere free from $\mathbf{H_2S}$. Ferrous sulphate paper may also be used for detection of $\mathbf{H_2S}$, but does not keep.

8. **Methyl Orange.**—Used as an internal indicator in acidimetry and alkalimetry. Turned red with acid and yellow with alkali. Can be used in the presence of carbonates to detect free alkali. Is acted upon by bicarbonate.

1 gm. of methyl orange is dissolved in 1 litre of water.

9. **Methyl Red.**—Used as an internal indicator like methyl orange, but is more sensitive.

1 gm. of methyl red is dissolved in 1 litre of water.

*Note.*—All test papers and solutions should be preserved in well-stoppered bottles.

## Inorganic Preparations, etc.

**Chlorine.**—Manganese dioxide is placed in a flask and just covered with conc. hydrochloric acid. On heating, a regular current of chlorine is obtained which is passed through water and through conc. sulphuric acid. Chlorine can also be prepared by heating a mixture of conc. hydrochloric acid (5 parts) with ground potassium dichromate (1 part). Another convenient method, which does not necessitate the use of heat, consists in treating good bleaching powder—cubes consisting of bleaching powder and plaster of Paris are sold for this purpose—with conc. hydrochloric acid.

**Bromine.**—When nascent bromine is required, a mixture of sodium bromide and bromate is added to the solution of the substance. The quantity of hydrochloric or of sulphuric acid required by the following equation is then added.

$$5NaBr + NaBrO_3 + 6H_2SO_4 = 6NaHSO_4 + 3H_2O + 6Br.$$

For most purposes commercial bromine is used, although this form sometimes contains as much as 10% of impurities, the chief of which is bromoform. It may be purified by shaking with conc. sulphuric acid.

**Hydrochloric Acid.**—Gaseous hydrochloric acid is conveniently prepared in a Kipp apparatus charged with fused ammonium chloride in lumps, and conc. sulphuric acid.

The most convenient method is to run concentrated hydrochloric acid from a dropping funnel (drawn to a capillary) underneath conc. sulphuric acid contained in a suction flask or other suitable vessel.

**Hydrobromic Acid.**—Sulphur dioxide is passed on to the surface of a mixture of 35 c.cs. of bromine and 200 c.cs. of water until a uniform pale yellow solution remains, which is distilled.

$$SO_2 + Br_2 + 2H_2O = 2HBr + H_2SO_4.$$

The distillate which may contain traces of sulphuric acid is redistilled over barium bromide.

When large quantities of hydrobromic acid are required, it is advisable to pass sulphur dioxide into a mixture of crushed ice and bromine until a uniform pale yellow solution is obtained.

**Hydriodic Acid.**—11 parts by weight of iodine are placed in a small round-bottomed flask, and 1 part of yellow phosphorus, cut into small pieces and dried, is gradually added. The addition of each piece causes a flash of light and the contents of the flask become liquid. When all the phosphorus has been added, solid phosphorus tri-iodide separates on cooling. The product is treated with $1\frac{1}{2}$ parts of water and, when gently heated, evolves hydrogen iodide, which is passed over some red phosphorus moistened with a little water in a **U**-tube. Heating is continued until the liquid just becomes colourless; otherwise, if heating is continued further, phosphine and phosphonium iodide are formed, which may cause explosion. If a solution of hydriodic acid is required, the gas is led through an inverted funnel into a small quantity of cold water. This solution, if dilute, may be concentrated by distillation. At 127° a solution of constant boiling point passes over, containing 57% of hydrogen iodide and of density 1·70.

For methoxyl and ethoxyl group estimations (p. 479) hydriodic acid (B.P. 127°) is distilled over phosphorus in a current of carbon dioxide.

**Ammonia.**—Ammonia gas can be conveniently obtained by gently heating conc. ammonium hydroxide solution (D. 0·88) which contains 35% of the gas. The evolved gas is dried by passing it over quicklime or soda-lime.

A very convenient method consists in dropping conc. ammonia solution on to solid caustic potash or soda packed in a drying tower or in a flask. If a relatively large quantity of alkali is used the gas evolved is dry.

**Zinc-Ammonium Chloride ($ZnCl_2.2NH_3$).**—This compound is formed by passing a current of dry ammonia gas into molten zinc chloride. It can also be obtained by passing the gas over pulverised anhydrous zinc chloride. This compound gives up ammonia on heating and is used in place of the concentrated solution in certain reactions.

**Anhydrous Aluminium Chloride.**—Aluminium shavings are freed from oil by boiling with alcohol, and then dried in an air bath at 120°. These are then packed in a thoroughly dry, hard glass tube, and kept in position

by asbestos plugs. To one end of the tube is attached a drying apparatus consisting of two sulphuric acid wash-bottles. To the other end is attached a receiving apparatus in the form of a wide-mouthed bottle, which is closed with a cork suitably bored to admit the hard glass tube and a calcium chloride tube. The air is displaced from the apparatus by passing a stream of hydrochloric acid from a Kipp apparatus through the drying apparatus. This is accomplished when the gas issuing from the calcium chloride tube of the receiver is completely soluble in water. The hard glass tube is heated in a small furnace, or by means of a few Ramsay burners, the heating being gradual at first, and commencing at the end nearer the hydrochloric acid generator. White vapours of aluminium chloride condense in the receiver, and it is necessary to maintain a rapid current of hydrochloric acid. The reaction is finished when there is only a small dark coloured residue of aluminium left in the tube. The aluminium chloride should be preserved in well-stoppered bottles (see p. 502), or in a desiccator. Aluminium chloride of reliable quality can now be purchased.

**Cuprous Chloride.**—100 gms. of crystallised copper sulphate, 48 gms. common salt and 200 c.cs. water are heated to boiling. 400 gms. of conc. hydrochloric acid and 72 gms. of copper turnings are added, and the whole is gently boiled until decolorised. It is important to exclude air from the flask, which may be done by using a plug of glass-wool or a Bunsen valve. The solution is rapidly decanted from unchanged copper, and then distilled water added until no more cuprous chloride is precipitated. The precipitate is filtered and washed, first with $\mathbf{SO_2}$ solution, and then with glacial acetic acid until the filtrate is colourless. It is removed from the filter and dried on a water bath until all the acetic acid is driven off. It is preserved in a well-stoppered bottle.

For the Sandmeyer reaction it is not necessary to isolate the solid product. The solution, after removing the copper, is treated with conc. hydrochloric acid until the total weight is 815 gms. This solution contains about 10% cuprous chloride.

Cuprous chloride can also be made by bubbling sulphur dioxide through a strong solution of cupric chloride and filtering off the white precipitate of the desired substance.

**Cuprous Bromide.**—100 gms. of crystallised copper sulphate, 288 gms. potassium bromide, 640 c.cs. of water, 160 gms. of copper turnings, and 88 gms. of conc. sulphuric acid are boiled until the whole is decolorised. The solution is decanted from unchanged copper.

**Lead Peroxide.**—100 gms. of bleaching powder are shaken up with 1,500 c.cs. of water and filtered. The filtrate is added gradually to a hot solution of 50 gms. lead acetate in 250 c.cs. of water; the addition is continued until the precipitate turns dark brown, and until no precipitate is formed by further addition of bleaching powder solution to a filtered test portion. The liquid is decanted, and the precipitate washed several times with water, then filtered and washed with water. It is preserved in a well-stoppered bottle in the form of a thick paste.

*Evaluation.*—0·5 to 1 gm. of the paste is treated (with cooling) with hydrochloric acid (approximately 15% solution). The chlorine liberated on heating is passed into a solution of 4 gms. of potassium iodide in water, and the iodine liberated is titrated with $\frac{N}{10}$ sodium thiosulphate. 1 c.c. of this thiosulphate solution is equivalent to 0·012 gm. of pure lead peroxide.

**Copper Powder.**—100 gms. of crystallised copper sulphate are dissolved in 350 gms. of water in a beaker, to which is attached a mechanical agitator. After cooling to laboratory temperature, the stirrer is set in motion, and 35 gms. (or more if necessary) of good quality zinc dust are gradually added until the solution is decolorised. The precipitated copper is washed by decantation with water. Dilute hydrochloric acid is added to the precipitate (to remove excess zinc), and agitation continued until evolution of hydrogen ceases. The powder is filtered off and preserved in a moist condition in a stoppered bottle.

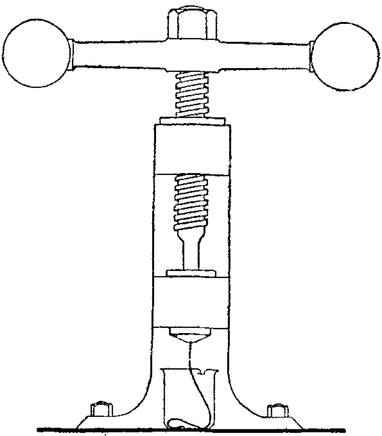


FIG. 84.

**Sodium Amalgam.**—*Weighing of Sodium.*—A lump of sodium is removed from a storage bottle and the surface cleaned with a knife. The bright lump is covered with petroleum ether (60°—80°) in a porcelain dish, and cut into small pieces. A second dish (or beaker) containing petroleum ether is weighed. Small lumps of sodium are removed from the first dish, quickly dried with filter paper, and added to the second until the required weight of sodium is obtained.

Sodium amalgam is usually made to contain $2\frac{1}{2}$% of sodium, as such a product is solid and easily pulverised.

Pure dry mercury is placed in a porcelain mortar and warmed in an oven to 60°—70°. It is then removed to a fume cupboard, and the metallic sodium removed a piece at a time from the petroleum ether, quickly dried with filter paper, and plunged under the surface of the mercury with a pointed glass rod. The hand should be covered with a towel during the operation. When preparing a large quantity of amalgam it is advisable to place only a portion of the mercury in the mortar at first, and to charge this with sodium before adding another portion of mercury to the contents. Proceeding in this way, the sodium dissolves quietly, and there is practically no spluttering with the second or later instalments of mercury. For a pure amalgam possessing special properties, see B., 61, (B), 876. See also O.S., VII, 89.

The usual way of introducing sodium into a liquid is in the

form of wire. A sketch of a press for this purpose is shown in Fig. 84.

**Silver Nitrite.**—A warm concentrated aqueous solution of silver nitrate containing 24 gms. is mixed with a warm concentrated solution of potassium nitrite containing 15 gms. The mixture is allowed to cool and the silver nitrite which separates filtered off and rapidly washed with water.

**Sodium Ethoxide (or Ethylate).**—100 c.cs. of absolute alcohol are placed in a flask and clean metallic sodium in small strips added until it no longer dissolves. Gentle heat is then applied to effect solution of the last particle of metal. The excess of alcohol is then distilled off up to 200°, and the dry residue warmed for some time in a current of hydrogen. It is then preserved in a well-stoppered bottle.

It is not always necessary to isolate the dry sodium ethoxide, the alcoholic solution being sufficient for most purposes.

A very reactive sodium ethylate can be obtained by adding the calculated quantity of absolute alcohol diluted with 2 vols. of dry xylene to granulated sodium under xylene (see below). During the addition the whole is well cooled and shaken. The xylene is then distilled off in a current of dry hydrogen.

**Alcoholic Potash.**—*Method I.*—10 gms. of caustic potash sticks are dissolved in an equal quantity of water and diluted with absolute alcohol to 400 c.cs. The solution is agitated with 10 gms. of anhydrous sodium sulphate until clarified, after which the clear solution is decanted.

*Method II.*—15 gms. of caustic potash sticks are agitated with 500 c.cs. of 90% alcohol at ordinary temperature until dissolved. After settling, the clear solution is decanted.

When the solution is required for analytical purposes, caustic potash "purified from alcohol" should be employed. The solution is standardised with hydrochloric acid, using phenolphthalein as indicator.

**Granulated Sodium.**—1 part of sodium is covered with 10 parts of dry xylene and heated to 120°. The flask is then corked and wrapped in a thick dry cloth and well shaken for a short time. The metal is thus obtained in the form of a powder. No more than 20 gms. of sodium should be granulated at one time. A dry bucket should be kept at hand to drop the flask into in case of breakage. (B., 21, 1464; 35, 3516; J. pr., [2], 54, 116; O.S., XIII, 23.)

**Anhydrous Sodium Acetate.**—Crystallised sodium acetate (**$CH_3.COONa.3H_2O$**) is heated in a basin over a small flame. The salt melts and for some time steam is evolved until all the water of crystallisation is driven off, at which stage the mass becomes solid. The flame is then increased, and heating continued until the mass melts again. Care must be taken not to char the product by using too large a flame. On cooling, the mass solidifies; it is broken up into small lumps and preserved in a stoppered bottle.

**Anhydrous Zinc Chloride.**—Crystallised zinc chloride is fused in a porcelain basin for a short time until no more steam is evolved, then

cooled and broken up into small pieces which are preserved in a well-stoppered bottle.

**Sodium Bisulphite.**—Sodium carbonate is covered with a layer of water—insufficient to dissolve it—and sulphur dioxide is passed into the mixture. After a time the solid disappears and an apple-green solution remains which smells strongly of sulphur dioxide. Sulphur dioxide may be obtained from a siphon of the liquid or generated by the action of conc. sulphuric acid on sodium sulphite.

Sodium bisulphite solution may be obtained by dissolving the sodium bisulphite in water, but the solution so prepared does not act so readily with aldehydes and ketones as the syrupy apple-green solution described above. A freshly prepared solution should always be used for aldehydes and ketones. A saturated solution of sodium metabisulphite ($\mathbf{Na_2S_2O_5}$) is also applicable.

**Sodamide.**—This is prepared by the action of ammonia gas on sodium heated to 300°—400°. For the preparation of quantities of 20 gms. or more the most convenient apparatus consists of some form of closed iron pot provided with inlet and outlet tubes for ammonia. The apparatus, Fig. 37, or an autoclave from which any copper fittings have been removed, can easily be adapted to suit the purpose. If the apparatus is free from rust, the sodium may be placed directly on the bottom of the pot. Or, it may be contained in a large nickel or iron crucible. Before commencing to heat, the air should be displaced from the pot by ammonia, after which the temperature is raised to and maintained at 300°—400° while a current of the dry gas is passed over the molten metal. The reaction takes place readily. If, after cooling and opening the pot, any soft lumps of sodium remain on the surface, these can be picked out with a knife, or else the apparatus may be closed again and more ammonia passed over the heated metal. The sodamide forms a hard mass which is chipped out with a knife or chisel. It is now available commercially and should be preserved in stoppered bottles.

**Evaluation of Zinc Dust.**—0·5 gm. of zinc dust is quickly weighed out and placed in a *dry* 250-c.c. graduated flask and 50 c.cs. of saturated solution of ferric alum added. The flask is stoppered and vigorously shaken until the zinc dust disappears. The reaction is represented by the equation—

$$Zn + Fe_2(SO_4)_3 = ZnSO_4 + 2FeSO_4.$$

25 c.cs. of conc. sulphuric acid are then added gradually, cooling being applied. When all the acid is added, the volume is made up to 250 c.cs. with distilled water. 50 c.cs. of this solution are then withdrawn and titrated with $\frac{N}{5}$ permanganate.

$$1 \text{ c.c. } \frac{N}{5}\, KMnO_4 \equiv 0{\cdot}00654 \text{ gm. Zn.}$$

**Sulphur Monochloride ($\mathbf{S_2Cl_2}$).**—In a dry retort are placed 100 gms. of sulphur, which are melted by gentle heating. The retort is connected to a receiver having an exit tube. Chlorine, dried by passing through

conc. sulphuric acid and fused calcium chloride, is passed into the melted sulphur. Sulphur monochloride distils over, and the passage of gas is continued until very little sulphur remains. The brownish-yellow liquid which collects is redistilled, the fraction 138°—139° being collected, and preserved in a sealed bottle.

**Sulphuryl Chloride ($SO_2Cl_2$).**—Dry sulphur dioxide is passed into a flask containing camphor and cooled in water, until it liquefies and no more gas is absorbed. Dry chlorine is now passed until absorption is complete, when sulphur dioxide is again passed, and so on, until the volume of liquid no longer increases. The liquid is then distilled, the fraction up to 100° being collected. This is then fractionated, collecting the colourless liquid, B.P. 70°.

Dry chlorine and sulphur dioxide when passed into sulphuryl chloride containing activated carbon combine to give sulphuryl chloride. (J. Eng., 16, 279.)

**Thionyl Chloride ($SOCl_2$).**—A mixture of carbonyl chloride and sulphur

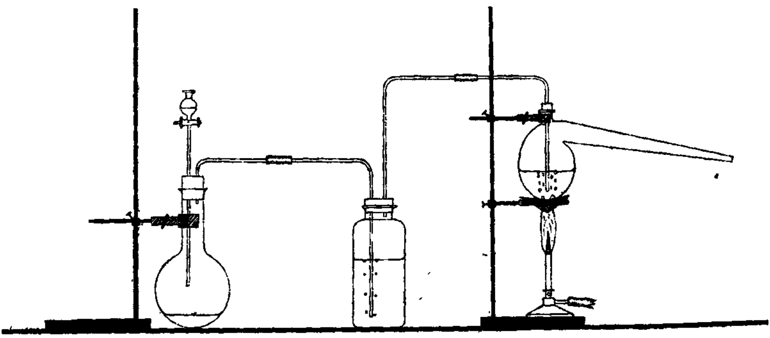


FIG. 85.

dioxide is passed over wood charcoal heated to above 200°. The liquid which distils is purified by distillation over dimethylaniline or quinoline. D° 1·677, B.P. 78·8°. (J. S. C. I., 45, 36, 55.)

**Phosphorus Di-iodide ($PI_2$).**—5 parts of phosphorus are dissolved in carbon disulphide, and to the well-cooled solution 41 parts of dry, powdered iodine are added. The carbon disulphide is then distilled off from the phosphorus di-iodide.

**Phosphorus Trisulphide ($P_2S_3$).**—The calculated quantities of dry amorphous phosphorus and sulphur are carefully melted together in a fireclay crucible. The product is then cooled and broken up.

**Chlorosulphonic Acid ($SO_3HCl$).**—A mixture of common salt and conc. hydrochloric acid is placed in a flask and hydrochloric acid gas produced by dropping conc. sulphuric acid on to it. The gas is dried and passed into fuming sulphuric acid in a retort until no further absorption takes place, cooling being applied to the retort, if necessary. The retort is then heated to 140°—153°, when chlorosulphonic acid distils over. A pure acid can be obtained, if necessary, by a further distillation,

the fraction boiling at 149°—151° being retained. The yield is nearly theoretical. Fig. 85 shows a convenient form of apparatus. A dilute chlorosulphonic acid can be readily obtained by adding common salt to fuming sulphuric acid.

**Fuming Nitric Acid.**—This can be prepared by distilling 2 mols. sodium nitrate with 1 mol. conc. sulphuric acid at over 200°; or by distilling a mixture of strong nitric acid and conc. sulphuric acid. The addition of 3—5% starch is effective. Its specific gravity at 15° is 1·533.

**Sodium Hypochlorite (NaOCl).**—1. Excess of sodium carbonate is added to a solution of bleaching powder. The filtrate, after removing the $CaCO_3$, contains the available chlorine, and the solution can be kept for some time.

2. Chlorine gas is passed into a cold solution of caustic soda until nearly all the soda is chlorinated. The solution is usually made to contain 14—15% available chlorine. (J. S. C. I., 18, 1096.)

**Sodium Hyposulphite** ("Hydrosulphite," $Na_2S_2O_4$).—$SO_2$ is passed into a strong solution of $NaHSO_3$ until saturated, and the mixture reduced with zinc dust.

$$NaHSO_3 + SO_2 + Zn = ZnSO_3 + Na_2S_2O_4 + H_2O.$$

Milk of lime is then added to precipitate **ZnO** and $CaSO_3$, and the liquor is saturated with salt at 50°, and cooled to crystallise the hyposulphite. By adding excess of caustic soda to a conc. solution of the crystals at 50°, the anhydrous salt is precipitated as a powder, which may be filtered and washed with alcohol.

Various hyposulphite compounds are used for industrial purposes including stable aldehyde compounds. Of these the formaldehyde compound (Formosul) is the most important, since it is the reducing agent almost universally employed in applying vat dyes by *printing* methods to textile materials. The less stable sodium "hydrosulphite" is used in *dyeing* with vat dyes. Stable zinc compounds (Rongalite) are also on the market.

**Ammonium Sulphite.**—$SO_2$ from a siphon is passed in a vigorous stream into 2 parts of conc. ammonia solution (D. 0·880) and 1 part of ice, surrounded by a freezing mixture. The solution gradually assumes a light yellow colour. When no more $SO_2$ is absorbed the solution is neutralised with conc. ammonia, giving a saturated solution of ammonium sulphite which sometimes deposits crystals on standing.

**Sodium Sulphide** ($Na_2S.9H_2O$).

*Evaluation.*—5 gms. sodium sulphide are dissolved in water up to 250 c.cs. and carefully neutralised with dilute acetic acid in presence of phenolphthalein until the latter is colourless. A $\frac{2}{5}$N solution of crystallised zinc sulphate (57·514 gms. $ZnSO_4.7H_2O$ per litre) is run in from a burette until all the soluble sodium sulphide is converted into zinc sulphide. A conc. solution of cadmium sulphate is spotted on thick blotting-paper, and a drop of the liquid being analysed is placed near it. A yellow stain will be produced as long as any soluble sulphide remains. The zinc sulphate is added until no yellow colour is given.

*Example.*— Volume of zinc sulphate = 9·3 c.cs.

$$\mathbf{Na_2S} \text{ in 25 c.cs.} = \frac{9{\cdot}3 \times 0{\cdot}078}{5} = 0{\cdot}1451 \text{ gm.}$$

$$\% \ \mathbf{Na_2S} = \frac{0{\cdot}1451 \times 10 \times 100}{5} = 29{\cdot}02.$$

**Carbonyl Chloride (Phosgene).**—100% sulphuric acid, to which is added 2% dry ignited kieselguhr, is placed in a flask which is attached to a small reflux condenser and a dropping funnel. Carbon tetrachloride is placed in the funnel, and from the top of the condenser is led a delivery tube passing through an empty wash-bottle, and then under the surface of toluene contained in a Buchner flask, the side tube of which is led to a draught duct. The sulphuric acid is heated to 140°, when the carbon tetrachloride is allowed to drop slowly. After the reaction commences the temperature may be lowered to about 120°, and this temperature maintained by gentle heat. The carbonyl chloride passes over and is absorbed in the toluene, while the hydrogen chloride which is formed passes over. The whole operation should be conducted in a good draught chamber as phosgene is very poisonous.

$$2H_2SO_4 + 3CCl_4 \rightarrow 3COCl_2 + 4HCl + S_2O_5Cl_2.$$

**Nitrous Fumes.**—Arsenious acid ($\mathbf{As_2O_3}$) is broken into small pieces and placed in a flask with a two-holed cork, which carries a dropping funnel and a delivery tube. The delivery tube is connected to an empty wash-bottle surrounded by cold water to condense any nitric acid which passes over. Nitric acid (D. 1·3) is dropped in gradually from the funnel, while the flask is gently heated ; a stream of nitrous fumes is readily evolved.

**Chromic Anhydride ($\mathbf{CrO_3}$).**—1·5 vols. of conc. sulphuric acid are added gradually, and with shaking, to 1 vol. of a saturated solution of potassium chromate. The mixture is allowed to cool, when the anhydride separates out as scarlet crystals. The crystals are filtered off, washed with a little nitric acid, and dried in a desiccator. The crystals are hygroscopic, and should be preserved in a well-stoppered bottle.

$$K_2CrO_4 + H_2SO_4 = K_2SO_4 + CrO_3 + H_2O.$$

**Chromyl Chloride ($\mathbf{CrO_2Cl_2}$).**—A mixture of 4 parts sodium chloride, 5 parts potassium dichromate and 9 parts fuming sulphuric acid is placed in a retort and distilled until coloured liquid no longer passes over. The chromyl chloride is then redistilled (B.P. 116°).

$$K_2Cr_2O_7 + 4NaCl + 3H_2SO_4.SO_3 = 2CrO_2Cl_2 + 2KHSO_4 + 4NaHSO_4.$$

**Anhydrous Stannous Chloride.**—Stannous chloride ($\mathbf{SnCl_2,2H_2O}$) (1 mol.) is treated with acetic anhydride (2 mols.). Dehydration is almost instantaneous, much heat is evolved and the anhydrous salt separates. When collected, and washed free of acetic acid with dry ether, it does not appear to be hygroscopic, and may be preserved indefinitely in a desiccator. It is readily soluble in acetone and in anhydrous methyl or ethyl alcohol ; insoluble in benzene or chloroform ; and it may be crystallised from acetic acid containing a little acetic anhydride. (For uses see p. 238 and J. C. S., 1931, 82.)

## Specific Gravities and Concentrations of Aqueous Acid Solutions.

| Hydrochloric. | | Nitric. | | Sulphuric. | | Acetic. | |
|---|---|---|---|---|---|---|---|
| % | D.[15] | % | D.[15] | % | D.[15] | % | D.[15] |
| 0·15 | 1·005 | 1·000 | 1·005 | 4·49 | 1·030 | 1·0 | 1·0007 |
| 2·14 | 1·010 | 1·90 | 1·010 | 10·19 | 1·070 | 5 | 1·0067 |
| 3·12 | 1·015 | 2·80 | 1·015 | 15·71 | 1·110 | 10 | 1·0142 |
| 4·13 | 1·020 | 3·70 | 1·020 | 20·91 | 1·150 | 15 | 1·0214 |
| 5·15 | 1·025 | 4·60 | 1·025 | 26·04 | 1·190 | 20 | 1·0284 |
| 6·15 | 1·030 | 5·50 | 1·030 | 31·11 | 1·230 | 25 | 1·0350 |
| 7·15 | 1·035 | 6·38 | 1·035 | 35·71 | 1·270 | 30 | 1·0412 |
| 8·16 | 1·040 | 7·26 | 1·040 | 40·35 | 1·310 | 35 | 1·0470 |
| 9·16 | 1·045 | 8.99 | 1·050 | 44·82 | 1·350 | 40 | 1·0523 |
| 10·17 | 1·050 | 9·84 | 1·055 | 50.11 | 1·400 | 45 | 1·0571 |
| 11·18 | 1·055 | 10·68 | 1·060 | 55·03 | 1·450 | 50 | 1·0615 |
| 12·19 | 1·060 | 11·51 | 1·065 | 60·65 | 1·510 | 55 | 1·0653 |
| 13·19 | 1·065 | 12·33 | 1·070 | 65·08 | 1·560 | 60 | 1·0685 |
| 14·17 | 1·070 | 13·95 | 1·080 | 70·32 | 1·620 | 65 | 1·0712 |
| 15·16 | 1·075 | 15·53 | 1·090 | 75·42 | 1·680 | 70 | 1·0733 |
| 16·15 | 1·080 | 17·11 | 1·100 | 80·68 | 1·740 | 75 | 1·0746 |
| 17·13 | 1·085 | 18·67 | 1·110 | 85·70 | 1·790 | 80 | 1·0748 |
| 18·11 | 1·090 | 22·30 | 1·120 | 90·05 | 1·820 | 85 | 1·0739 |
| 19·06 | 1·095 | 22·54 | 1·135 | 90·40 | 1·822 | 90 | 1·0713 |
| 20·01 | 1·100 | 24·08 | 1·145 | 91·00 | 1·825 | 91 | 1·0705 |
| 20·97 | 1·105 | 26·36 | 1·160 | 91·50 | 1·827 | 92 | 1·0696 |
| 21·92 | 1·110 | 28·63 | 1·175 | 92·10 | 1·830 | 93 | 1·0680 |
| 22·86 | 1·115 | 31·30 | 1·185 | 92·52 | 1·832 | 94 | 1·0674 |
| 23·82 | 1·120 | 32·36 | 1·200 | 93·05 | 1·834 | 95 | 1·0660 |
| 24·78 | 1·125 | 34·55 | 1·215 | 93·43 | 1·835 | 96 | 1·0644 |
| 25·75 | 1·130 | 36·78 | 1·230 | 94·20 | 1·837 | 97 | 1·0625 |
| 26·70 | 1·135 | 39·05 | 1·245 | 94·60 | 1·838 | 98 | 1·0604 |
| 27·66 | 1·140 | 41·34 | 1·260 | 95·00 | 1·839 | 99 | 1·0580 |
| 28·61 | 1·145 | 44·41 | 1·280 | 95·60 | 1·840 | 100 | 1·0553 |
| 29·57 | 1·150 | 46·72 | 1·295 | 95·95 | 1·8405 | | |
| 30·55 | 1·155 | 49·07 | 1·310 | 97·00 | 1·8410 | | |
| 31·52 | 1·160 | 52·37 | 1·330 | 97·70 | 1·8415 | | |
| 32·49 | 1·165 | 55·79 | 1·350 | 98·20 | 1·8410 | | |
| 33·46 | 1·170 | 58·48 | 1·365 | 98·70 | 1·8405 | | |
| 34·42 | 1·175 | 61·27 | 1·380 | 99·20 | 1·8400 | | |
| 35·39 | 1·180 | 63·23 | 1·390 | 99·45 | 1·8395 | | |
| | | 65·30 | 1·400 | 99·70 | 1·8390 | | |
| | | 67·50 | 1·410 | 99·95 | 1·8385 | | |
| | | 69·80 | 1·420 | | | | |

## Specific Gravities and Concentrations of Aqueous Alkaline Solutions.

| Caustic Soda. | | Caustic Potash. | | Ammonia. | |
|---|---|---|---|---|---|
| % | D.[15] | % | D.[15] | % | D.[15] |
| 0·61 | 1·007 | 1 | 1·009 | 0·45 | 0·998 |
| 2·00 | 1·022 | 3 | 1·025 | 1·37 | 0·994 |
| 3·35 | 1·036 | 5 | 1·041 | 2·31 | 0·990 |
| 4·26 | 1·052 | 7 | 1·058 | 3·30 | 0·986 |

## Specific Gravities and Concentrations of Aqueous Alkaline Solutions—*continued.*

| Caustic Soda. | | Caustic Potash. | | Ammonia. | |
|---|---|---|---|---|---|
| % | D.[15] | % | D.[15] | % | D.[15] |
| 5·87 | 1·067 | 9 | 1·074 | 4·30 | 0·982 |
| 6·55 | 1·075 | 11 | 1·092 | 5·30 | 0·978 |
| 7·31 | 1·083 | 13 | 1·110 | 6·30 | 0·974 |
| 8·68 | 1·100 | 15 | 1·128 | 7·31 | 0·970 |
| 9·42 | 1·108 | 17 | 1·146 | 8·33 | 0·966 |
| 10·97 | 1·125 | 19 | 1·166 | 9·35 | 0·962 |
| 12·64 | 1·142 | 21 | 1·188 | 10·47 | 0·958 |
| 14·37 | 1·162 | 23 | 1·209 | 11·60 | 0·954 |
| 15·91 | 1·180 | 25 | 1·230 | 12·74 | 0·950 |
| 16·77 | 1·190 | 27 | 1·252 | 13·88 | 0·946 |
| 17·67 | 1·200 | 29 | 1·276 | 14·46 | 0·944 |
| 19·58 | 1·220 | 31 | 1·300 | 15·04 | 0·942 |
| 21·42 | 1·241 | 33 | 1·324 | 15·63 | 0·940 |
| 23·67 | 1·263 | 35 | 1·349 | 16·82 | 0·936 |
| 25·80 | 1·285 | 37 | 1·374 | 18·03 | 0·932 |
| 27·80 | 1·308 | 39 | 1·400 | 19·25 | 0·928 |
| 29·93 | 1·332 | 41 | 1·425 | 20·49 | 0·924 |
| 32·47 | 1·357 | 43 | 1·450 | 21·75 | 0·920 |
| 34·96 | 1·383 | 45 | 1·475 | 23·03 | 0·916 |
| 36·25 | 1·397 | 47 | 1·499 | 24·33 | 0·912 |
| 37·47 | 1·410 | 49 | 1·525 | 25·65 | 0·908 |
| 38·80 | 1·424 | 51 | 1·552 | 26·98 | 0·904 |
| 39·99 | 1·438 | 53 | 1·578 | 28·33 | 0·900 |
| 41·41 | 1·453 | 55 | 1·604 | 29·69 | 0·896 |
| 42·83 | 1·468 | 57 | 1·630 | 30·37 | 0·894 |
| 44·38 | 1·483 | 59 | 1·655 | 31·75 | 0·890 |
| 46·15 | 1·498 | 61 | 1·681 | 32·50 | 0·888 |
| 47·60 | 1·514 | 63 | 1·705 | 33·25 | 0·886 |
| 49·02 | 1·530 | 65 | 1·729 | 34·95 | 0·882 |
| | | 67 | 1·754 | | |
| | | 69 | 1·780 | | |

## Vapour Pressures.

| Vapour pressure of water at different temperatures. | | | | Vapour pressure of conc. KOH solution at different temperatures. | | |
|---|---|---|---|---|---|---|
| Temperature | Pressure. | Temperature. | Pressure. | Temperature. | 40 gms. KOH : 100 c.c. $H_2O$. | 49 gms. KOH : 100 c.c. $H_2O$. |
| | mms. | | mms. | | mms. | mms. |
| 0° | 4·6 | 16° | 13·5 | 10° | 6·5 | 5·6 |
| 2° | 5·3 | 18° | 15·4 | 12° | 7·5 | 6·5 |
| 4° | 6·1 | 20° | 17·4 | 14° | 8·4 | 7·3 |
| 6° | 7·0 | 22° | 19·7 | 16° | 9·6 | 8·3 |
| 8° | 8·0 | 24° | 22·2 | 18° | 10·9 | 9·5 |
| 10° | 9·2 | 26° | 25·0 | 20° | 12·4 | 10·8 |
| 12° | 10·5 | 28° | 28·1 | 22° | 13·9 | 12·1 |
| 14° | 11·9 | 30° | 31·6 | | | |

## Table of Approximate Atomic Weights
($O = 16$)

| Element. | | Approximate Atomic Weight. | Element. | | Approximate Atomic Weight. |
|---|---|---|---|---|---|
| Aluminium | **Al** | 27 | Lithium | **Li** | 7 |
| Antimony | **Sb** | 120 | Magnesium | **Mg** | 24·5 |
| Arsenic | **As** | 75 | Manganese | **Mn** | 55 |
| Barium | **Ba** | 137·5 | Mercury | **Hg** | 200·5 |
| Bismuth | **Bi** | 208 | Molybdenum | **Mo** | 96 |
| Boron | **B** | 11 | Nickel | **Ni** | 58·5 |
| Bromine | **Br** | 80 | Nitrogen | **N** | 14 |
| Cadmium | **Cd** | 112·5 | Oxygen | **O** | 16 |
| Caesium | **Cs** | 133 | Palladium | **Pd** | 107 |
| Calcium | **Ca** | 40 | Phosphorus | **P** | 31 |
| Carbon | **C** | 12 | Platinum | **Pt** | 195 |
| Chlorine | **Cl** | 35·5 | Potassium | **K** | 39 |
| Chromium | **Cr** | 52 | Silicon | **Si** | 28 |
| Cobalt | **Co** | 59 | Silver | **Ag** | 108 |
| Copper | **Cu** | 63·5 | Sodium | **Na** | 23 |
| Fluorine | **F** | 19 | Strontium | **Sr** | 87·5 |
| Gold | **Au** | 197 | Sulphur | **S** | 32 |
| Hydrogen | **H** | 1 | Tin | **Sn** | 119 |
| Iodine | **I** | 127 | Titanium | **Ti** | 48 |
| Iron | **Fe** | 56 | Vanadium | **V** | 51 |
| Lead | **Pb** | 207 | Zinc | **Zn** | 65·5 |

# CHAPTER XLIII

## TESTS FOR COMMON ORGANIC ACIDS, ALKALOIDS, CARBOHYDRATES

### Preliminary Tests

**I. Effect of Heat.**—Heat about 0·25 gm. on a crucible lid—carefully at first, noting any odour evolved and whether the substance chars with or without melting. If the substance chars, as many organic compounds do, continue the heating, using the blowpipe if necessary, until all the carbon is burnt away. Note any flame tests.

Melts, vaporises, vapours may catch fire—oxalic, benzoic or salicylic acid.

Chars and emits odour of burnt sugar—carbohydrate, tartrate.

Ammonia evolved—ammonium salt.

Coloured residue—salt of metal giving coloured oxide.

White residue—salt of metal giving white oxide or carbonate. Touch residue with moist litmus paper; an alkaline reaction indicates presence of **Na, K, Li, Ca, Ba, Sr** or **Mg.**

Organic salts of **Hg, As,** and **$NH_4$** volatilise completely on ignition.

**II. Heat in a Dry Test Tube.**—Note evolution of odour or inflammable gas.

Cyanogen evolved, burns with a peach coloured flame—cyanide of **Hg** or **Ag.**

Melts and forms a sublimate—oxalic, benzoic or salicylic acid.

Odour of benzene evolved—benzoate.

Odour of phenol evolved—salicylate.

Chars, emits odour of burnt sugar—carbohydrate, glucoside, tartrate.

Chars, evolves irritating fumes—citrate.

Chars, emits tarry odour—alkaloid.

**III. Test Reaction of Substance to moist litmus and its Solubility in water.**—Free acids and some acid salts—acidic.

Benzoic and salicylic acids—soluble on heating, crystallise on cooling.

Alkaloids—sparingly soluble, alkaline.

Alkaloid salts—usually soluble and acidic.

Starch—insoluble in cold, opalescent solution on boiling.

**IV. Heat with dilute Sulphuric Acid.**—Odour of formic acid, acetic acid—formates, acetates respectively.

Odour of hydrocyanic acid—cyanide, ferro- or ferri-cyanide.

Crystals, soluble in alkali, separate on cooling—benzoate, salicylate.

Precipitate after boiling and cooling—salicin.

**V. Treat with conc. Sulphuric Acid.**—If there is no apparent action heat the mixture.

Deep red coloration in the cold—glucoside.

Odour of acetic acid on warming—acetate.

Charring with odour of burnt sugar on warming—carbohydrate, tartrate.

Carbon monoxide (test inflammability) on heating, no charring—formate, cyanide, ferrocyanide, ferricyanide.

Carbon monoxide and carbon dioxide (test with lime water) on heating, no charring—oxalate.

**VI. Heat with Caustic Soda Solution.**—Ammonia evolved—ammonium salt.

Substance (sparingly soluble in water) dissolves—benzoic, salicylic acid.

Substance (soluble in water) yields precipitate—salt of alkaloid.

Soluble, resinifies on warming—glucose, lactose.

**VII. Heat with Soda-lime.**—Grind about 0·5 gm. with 2 gms. soda-lime in a mortar. Transfer to small hard glass tube, cover with a layer of ground soda-lime and heat. Detect odour and inflammability of any gases evolved.

Ammonia evolved—ammonium salt, alkaloid.

Phenol evolved—salicylic acid, salicylate.

Benzene evolved—benzoic acid, benzoate.

Inflammable gas—formate, acetate, oxalate.

## Organic Acids

Aqueous solutions of calcium chloride, ferric chloride or silver nitrate give precipitates or colorations with certain organic acids which are valuable for the detection of these acids. It is important to use neutral solutions of the acids which at the same time do not contain metallic radicles likely to react with the reagents added. Thus the addition of calcium chloride to a solution of lead acetate may produce a precipitate of lead chloride. A neutral solution, which should be of about 10% concentration, prepared as follows, usually avoids such complications :—

*Neutral Solution.*—If the acid is combined with a metal other than an alkali metal or ammonia, about 2 gms. of the compound are boiled with 10 c.cs. concentrated sodium carbonate solution. Metals which would otherwise interfere during the tests with the above reagents will remain undissolved or be precipitated in the form of their hydroxides or carbonates. The precipitate is filtered off and examined for metals. The filtrate is acidified with a slight excess of nitric acid (testing with litmus), boiled to expel carbon dioxide, then made slightly alkaline with ammonia and finally boiled to expel this excess of ammonia. Portions of this neutral solution are taken for the appropriate tests. Neutral solutions from free acids are conveniently prepared by dissolving in a slight excess of ammonia and boiling off the latter.

**Solubility of Salts.**—The calcium salts of oxalic and tartaric acids are very sparingly soluble in cold water, calcium citrate is sparingly soluble in hot water. In some instances, as in the analysis of mixtures where an

acid is present in low concentration, it may be advisable to add solid calcium chloride.

The ferric salts of benzoic, succinic, hydroferrocyanic, gallic and tannic acids are sparingly soluble in cold water, while basic ferric salts of formic and acetic acids formed on boiling are also sparingly soluble. Solutions of ferric thiocyanate and salicylate exhibit characteristic colorations.

A number of acids form sparingly soluble silver salts. Formates and tartrates reduce ammoniacal silver nitrate.

**Oxalic, $COOH.COOH + 2H_2O$.**—White crystalline solid. Loses $2H_2O$ at 100°, then melts and sublimes partly with decomposition, giving off $CO_2$ and **H.COOH.** Easily soluble in water and in alcohol.

Oxalic acid and oxalates give with—

Conc. $H_2SO_4$, on heating, usually no charring ; **CO** and $CO_2$ evolved.

Neutral solutions of oxalates give with—

1. $CaCl_2$, white precipitate—$CaC_2O_4$, soluble in **HCl** and $HNO_3$, almost insoluble in acetic acid.
2. $AgNO_3$, white precipitate—$Ag_2C_2O_4$, soluble in $HNO_3$ and ammonia.
3. $KMnO_4$ in dilute $H_2SO_4$ solution, decolorised and $CO_2$ given off.

**Tartaric, COOH.CH(OH).CH(OH).COOH.**

Colourless crystals. M.P. 167°—170°.

Readily soluble in water, moderately in alcohol, sparingly in ether.

Tartaric acid and tartrates :—

1. On heating, charring takes place ; burnt sugar smell, and acid vapours evolved.
2. With conc. $H_2SO_4$, on heating, turn brown then black, and acid vapours evolved.

Neutral solutions of tartrates give with—

1. $CaCl_2$, white precipitate—$CaC_4H_4O_6$, usually only after vigorous shaking ; soluble in **HCl**, $HNO_3$ and, if precipitate has not assumed the crystalline form, in acetic acid.
2. $AgNO_3$, white precipitate—$Ag_2C_4H_4O_6$, soluble in $HNO_3$, and ammonia. Precipitate dissolved in minimum quantity of ammonia, with addition of crystal of $AgNO_3$, deposits silver mirror on gently heating.
3. Small crystal of $FeSO_4$, two drops of $H_2O_2$ solution, and making strongly alkaline (Fenton's reagent)—violet coloration.

**Citric, $COOH.CH_2.C(OH)(COOH).CH_2.COOH + H_2O$.**

Colourless crystals ; M.P. 100° (anhydrous acid, M.P. 153°) ; readily soluble in water and alcohol, sparingly in ether. On heating, melts and gives off water and acid vapours ; no smell of burnt sugar.

Citric acid and citrates, in the solid, on heating with conc. $H_2SO_4$ for 10 minutes at 90°—95° effervesce and give yellow solutions, which after dilution and making alkaline give red coloration with nitroprusside solution due to acetone or its carboxylic acid.

Neutral solutions of citrates give with—

1. $CaCl_2$ on boiling, white precipitate—$Ca_3(H_6H_5O_7)_2$ ; no precipitate in the cold.

2. **$AgNO_3$**, white precipitate—**$Ag_3C_6H_5O_7$**, soluble in ammonia. No mirror formed as in tartrates.

3. **$Ca(OH)_2$** on boiling, white precipitate—**$Ca_3(C_6H_5O_7)_2$**, which redissolves on cooling.

4. 5 gms. **$HgSO_4$** are dissolved in dil. **$H_2SO_4$** (20 c.cs. conc. acid, 100 c.cs. water). A mixture of 1 c.c. of this solution with 5 c.cs. of dil. citrate solution decolorises dil. **$KMnO_4$** with formation of white ppt. (Denigès' test).

**Benzoic, $C_6H_5COOH$.**—White needles or scales; M.P. 121°; sparingly soluble in cold, fairly readily in boiling water; readily soluble in alcohol and in ether. On heating, melts and volatilises.

All benzoates give benzoic acid with mineral acids.

On heating acid or salts with soda-lime, benzene evolved.

Conc. **$H_2SO_4$**, on heating, dissolves; no charring; acid precipitated on dilution with water.

Neutral solutions of benzoates give with—

1. **$CaCl_2$**, no precipitate even on addition of alcohol.

2. **$FeCl_3$**, buff precipitate—**$Fe(C_7H_5O_2)_3$**, soluble in **HCl** with liberation of benzoic acid.

3. **HCl,** free acid precipitated.

**Succinic, $COOH.CH_2CH_2.COOH$.**—Colourless prisms; M.P. 181°; soluble in water, sparingly soluble in cold alcohol and ether.

On heating, loses water, yielding anhydride.

Succinates char at high temperature.

Conc. **$H_2SO_4$** added to succinates and heated, solution turns dark and sublimate forms on cold part of dry tube.

Neutral solutions of succinates give with—

1. **$CaCl_2$**, no precipitate even on boiling.

2. **$FeCl_3$**, brownish-red precipitate of basic ferric succinate easily soluble in **HCl.**

3. **$BaCl_2$** in presence of ammonia, white precipitate on addition of alcohol.

**Formic, H.COOH.**—Colourless liquid; M.P. 8°; B.P. 101°. Pungent odour; vapour burns with blue flame. Miscible in all proportions with water, alcohol and ether.

Formates, when heated, evolve **CO,** yielding carbonates, oxides or metals.

Conc. **$H_2SO_4$**, **CO** evolved on heating.

Neutral solutions of formates give with—

1. **$FeCl_3$**, red coloration, which on boiling yields reddish precipitate of basic ferric formate.

2. **$AgNO_3$** in conc. solutions, white precipitate—**$AgCHO_2$**, turning dark even in cold, owing to deposition of metallic silver. This decomposition of silver formate does not take place in presence of excess ammonia.

3. **$HgCl_2$**, on warming, white precipitate—**$Hg_2Cl_2$**, or grey precipitate of metallic mercury.

4. Formates or formic acid decolorise **$KMnO_4$** solution.

5. Solutions of formates or formic acid, with few drops alcohol and few drops conc. **$H_2SO_4$**, on warming, give ethyl formate, recognised by sweet smell.

**Acetic, $CH_3.COOH$.**—Colourless crystals; M.P. 17°; B.P. 119°; characteristic odour; vapour burns with bluish flame; miscible in all proportions with water, alcohol and ether.

Acetates, when heated alone, give acetone, with conc. **$H_2SO_4$**, acetic acid.

Solid acetates with conc. **$H_2SO_4$** and a few drops of alcohol, on heating, give ethyl acetate, recognised by pleasant odour.

Dry acetates mixed with a trace of **$As_2O_3$**, when heated, give vapours of cacodyl oxide, **$As_2(CH_3)_4O$**, recognised by smell (*caution!* vapours are very poisonous).

Neutral solutions of acetates give with—

1. **$FeCl_3$**, red coloration, which on boiling yields brownish precipitate of basic ferric acetate. The red colour is destroyed by **HCl**, but not by **$HgCl_2$**.

2. **$AgNO_3$** in conc. solutions, white crystalline precipitate—**$AgC_2H_3O_2$**, soluble in hot water and in ammonia. Silver acetate is not reduced when the solution is boiled.

**Hydrocyanic, HCN.**—Colourless volatile liquid; B.P. 26°; burns with reddish-violet flame; soluble in water, alcohol and ether. Aqueous solution does not redden blue litmus.

Cyanides with conc. **$H_2SO_4$**, on heating, liberate **CO.**

Dilute **HCl**, in cold, liberates **HCN**, recognised by smell (*caution!*).

Solutions of cyanides give with—

1. **$AgNO_3$**, white precipitate—**AgCN**, insoluble in dilute **$HNO_3$**, soluble in ammonia and **KCN** solution.

2. **NaOH** with few drops **$FeSO_4$** and **$FeCl_3$** solutions, acidified with **HCl**, precipitate of Prussian blue.

3. Yellow ammonium sulphide, on evaporation to dryness—thiocyanate, which gives with **$FeCl_3$** in dilute **HCl** deep red colour.

**Cyanic, HCNO.**—Unstable liquid; smell similar to acetic acid.

Cyanates with **HCl** give **$CO_2$** and **$NH_4Cl$.**

Aqueous solution of **KCNO** on standing gives **$NH_3$**, leaving **$K_2CO_3$** in solution.

Solutions of cyanates give with **$AgNO_3$**, white precipitate—**AgCNO**, soluble in ammonia; decomposed by acids with liberation of **$CO_2$** and formation of an ammonium salt.

For conversion to urea, see p. 436.

**Thiocyanic, HCNS.**—Unstable liquid; salts are decomposed when heated.

Solid salts heated with **$H_2SO_4$** yield **$CO_2$**, **HCN** and **$H_2S$.**

Solutions of thiocyanates give with—

1. **$AgNO_3$**, white precipitate—**AgCNS**, insoluble in dilute **$HNO_3$**, sparingly soluble in ammonia; also soluble in **KCNS.**

2. **$FeCl_3$** to dilute solution, deep red coloration—**$Fe(CNS)_3$**, colour is unchanged by **HCl,** but destroyed by **$HgCl_2$**.

For conversion to thiourea, see p. 436.

**Hydroferrocyanic, $H_4Fe(CN)_6$**.—Colourless crystalline solid, readily soluble in water.

All ferrocyanides are decomposed by heat.

Conc. **$H_2SO_4$**, on heating, **CO** evolved.

Solutions of ferrocyanides give with—

1. **$FeCl_3$**, dark blue precipitate—Prussian blue, **$Fe_4\{Fe(CN)_6\}_3$**, insoluble in **HCl,** soluble in oxalic acid.
2. **$FeSO_4$**, pale blue precipitate, which rapidly darkens on exposure to air.
3. **$AgNO_3$**, white precipitate—**$Ag_4Fe(CN)_6$**, insoluble in dilute **$HNO_3$** and in ammonia, soluble in **KCN.**
4. **$CuSO_4$**, brown precipitate—**$Cu_2Fe(CN)_6$**, insoluble in dilute acids.

**Hydroferricyanic, $H_3Fe(CN)_6$**.—Yellow crystalline solid, readily soluble in water.

All metallic ferricyanides are decomposed by heat.

Conc. **$H_2SO_4$**, on heating, **CO** and **$CO_2$**.

Solutions of ferricyanides give with—

1. **$FeCl_3$**, brown or dark green coloration.
2. **$FeSO_4$**, dark blue precipitate—Turnbull's blue, **$Fe_3\{Fe(CN)_6\}_2$**, insoluble in acids, decomposed by **KOH.**
3. **$CuSO_4$**, greenish-yellow precipitate—**$Cu_3\{Fe(CN)_6\}_2$**.
4. **$AgNO_3$**, orange precipitate—**$Ag_3Fe(CN)_6$**, insoluble in dilute **$HNO_3$**, soluble in ammonia and **KCN.**

**Salicylic, $C_6H_4OH.COOH$** [1 : 2].—Colourless needles; M.P. 157°; sparingly soluble in cold, moderately in hot water; easily soluble in alcohol and in ether.

Salicylates give salicylic acid with mineral acids. When strongly heated gives **$CO_2$** and phenol. Salicylic acid or salicylates mixed with soda-lime and heated give phenol, recognised by its smell.

The acid is soluble in conc. **$H_2SO_4$**, and is reprecipitated on dilution with water.

Dry salicylates, with few drops methyl alcohol and conc. **$H_2SO_4$**, on warming, methyl salicylate (oil of winter green); recognised by smell.

Neutral solutions of salicylates give with—

1. **$FeCl_3$**, violet coloration; colour destroyed by acids or alkalis.
2. Bromine water, yellowish-white precipitate.

**Uric, $C_5H_4N_4O_3$**.—White crystalline powder; sparingly soluble in water and all solvents; insoluble in cold **$Na_2CO_3$**, but soluble in **NaOH.** On heating, **$NH_3$**, **HCNO, HCN** and urea are formed.

Conc. **$H_2SO_4$**, in cold, soluble; on heating, **$CO_2$** and **$SO_2$** evolved.

*The Murexide Test.*—Evaporate a little uric acid and dilute **$HNO_3$** to dryness. Add few drops of ammonia to the red residue when cold; purple coloration. Uric acid reduces Fehling's solution on prolonged boiling.

**Tannic (Gallo-tannic), $C_{14}H_{10}O_9 + 2H_2O$.**—Colourless, amorphous, glistening mass ; decomposes on heating ; very soluble in hot water.

Action of caustic alkalis same as for gallic acid.

Conc. $H_2SO_4$, on warming, dark green coloration, and brownish-black precipitate on dilution.

Neutral solutions of tannates give with—

1. $FeCl_3$, bluish-black precipitate, soluble in **HCl**, but reprecipitated by ammonia.
2. **KCN,** no coloration.
3. Tartar emetic, precipitate.
4. Gelatin, greyish precipitate.
5. $AgNO_3$, metallic silver.
6. $NH_4Cl$ and ammonia, precipitate.

**Gallic, $C_6H_2(OH)_3COOH$** [3 : 4 : 5 : 1].—Colourless, silky needles ; decomposes on heating, giving pyrogallol and leaving charred residue ; sparingly soluble in cold water ; readily soluble in hot water, and in alcohol.

Gallates when mixed with caustic alkalis oxidise in air, giving coloured solutions.

Conc. $H_2SO_4$, on warming, dark red solution, and dark red precipitate on dilution with water.

Neutral solutions of gallates give with—

1. $FeCl_3$, bluish-black precipitate, soluble in excess to a green solution, also soluble in **HCl.**
2. **KCN,** pink coloration, which disappears on standing and reappears on shaking.
3. Solution of gelatin, no precipitate.
4. Fehling's solution, precipitate of $Cu_2O$.
5. $AgNO_3$, metallic silver.
6. $NH_4Cl$ and ammonia, no precipitate.

**Lactic, $CH_3.CHOH.COOH$.**—Syrupy liquid ; decomposes on heating, giving acetaldehyde.

Lactic acid and lactates—

1. On warming with conc. $H_2SO_4$, effervesce, and acetaldehyde evolved ; solution darkens.
2. On warming with iodine dissolved in **KI,** and adding **NaOH** to make alkaline, give iodoform.

Neutral solutions of lactates give with—

1. $AgNO_3$, no precipitate.
2. $CaCl_2$, no precipitate.
3. $KMnO_4$ acidified, on warming, decoloration.

## Alkaloids

Most of the alkaloids, with the exception of coniine and nicotine, are crystalline solids ; they are usually insoluble or sparingly soluble in water, but being basic they dissolve in acids forming soluble salts, from which the base is usually precipitated by dilute **NaOH** or $Na_2CO_3$. In a few cases, *e.g.*, morphine, the alkaloid is soluble in excess of alkali, while

the solubility in water of a base such as nicotine prevents its precipitation by the addition of alkali to solutions of its salts. The liquid alkaloids coniine and nicotine are volatile in steam.

The majority are optically active and possess a bitter astringent taste, as well as an extremely poisonous character.

Alkaloids in general give precipitates with certain reagents amongst which may be mentioned :—

1. Solution of iodine in **KI**—brown amorphous ppt.
2. Nessler's solution—white or discoloured amorphous ppt.
3. Potassium mercuric iodide—white or yellowish-white ppt.
4. Phosphomolybdic acid—light to brownish-yellow gelatinous ppt.
5. Chloroplatinic acid—yellow crystalline solid.
6. Tannic acid or picric acid in aqueous solution—almost all the alkaloids ppt.
7. Hydroferro- and hydroferri-cyanic acids—yellow ppts.

Some give definite colorations with oxidising agents, *e.g.*, conc. $H_2SO_4$ and $K_2Cr_2O_7$. The hydroferro- and hydroferri-cyanides are usually of definite crystalline form under the microscope, while the picrates and picrolonates usually possess the added advantage of a definite melting point.

**Morphine, $C_{17}H_{19}O_3N + H_2O$.**—White amorphous or crystalline substance, sparingly soluble in cold water and in ether; soluble in **NaOH** solution; M.P. 230°.

1. Conc. $H_2SO_4$—Pale orange solution.
2. Conc. $H_2SO_4$ + crystal of $K_2Cr_2O_7$—Greenish-brown coloration.
3. Conc. $H_2SO_4$ containing a few drops $HNO_3$—A violet coloration on standing.
4. Conc. $HNO_3$—Red coloration, changing to yellow on warming.
5. One drop of formalin in 1 c.c. conc. $H_2SO_4$—Purple colour, changing to blue.
6. Solid $Na_3AsO_4$—Slate-blue coloration.

To aqueous solution of salt add—

1. **NaOH**—Base precipitated, soluble in excess.
2. $FeCl_3$ (neutral solution)—Blue coloration.
3. $KIO_3$ crystal and warm—Iodine liberated; cool and test with starch.

**Cinchonine.**—$C_{19}H_{22}ON_2$.—White powder or crystalline compound; almost insoluble in water; *d*-rotatory; M.P. 255°.

Solutions of salts do not exhibit fluorescence.

1. Conc. $H_2SO_4$—Pale green solution.
2. Conc. $H_2SO_4$ + crystal of $K_2Cr_2O_7$—Olive green coloration.

To aqueous solution of salt add—

1. **NaOH**—Base precipitated, insoluble in excess.
2. $K_4Fe(CN)_6$ to neutral or slightly acid solution—Yellowish-white ppt., soluble in excess on warming.

**Quinine, $C_{20}H_{24}O_2N_2 + 3H_2O$.**—White powder (anhydrous) or crystalline compound; sparingly soluble in water; *l*-rotatory; M.P. 177°

(anhydrous) or 67° (hydrated). Dilute solutions of its salts, acidified with $\mathbf{H_2SO_4}$, exhibit a bluish fluorescence in daylight, which is discharged by **HCl.**

1. Conc. $\mathbf{H_2SO_4}$—Pale green solution.
2. Conc. $\mathbf{H_2SO_4}$ + crystal of $\mathbf{K_2Cr_2O_7}$—Dark olive green coloration.

To aqueous solution of salt add—

1. Conc. chlorine water ($\frac{1}{5}$ its volume), and then excess of conc. $\mathbf{NH_4OH}$—Emerald green colour.
2. Chlorine water, $\mathbf{K_4Fe(CN)_6}$ and $\mathbf{NH_4OH}$—Red coloration. Quinine hydrochloride, on heating alone, assumes a violet colour, and gives off violet vapours.

**Strychnine,** $\mathbf{C_{21}H_{22}O_2N_2}$.—Colourless needles; M.P. 268°; sparingly soluble in water, alcohol, and ether; very soluble in $\mathbf{CHCl_3}$; *l*-rotatory in alcohol.

1. Conc. $\mathbf{H_2SO_4}$—Colourless solution (even at 100°).
2. Conc. $\mathbf{H_2SO_4}$ + crystal of $\mathbf{K_2Cr_2O_7}$—Bluish-violet coloration.

To solution of salt add—

1. **NaOH**—Base precipitated, soluble in excess of $\mathbf{NH_4OH}$.
2. $\mathbf{K_3Fe(CN)_6}$ or $\mathbf{K_2CrO_4}$—Yellow crystalline ppt. in neutral and fairly conc. strychnine salt solution.

**Brucine,** $\mathbf{C_{23}H_{26}O_4N_2 + 4H_2O}$.—Colourless needles or prisms; M.P. 168°; sparingly soluble in water, readily soluble in alcohol and in chloroform; $[\alpha]_D$ = about − 120° (in $\mathbf{CHCl_3}$).

1. Conc. $\mathbf{H_2SO_4}$—Rose-red coloration, changing to yellow.
2. Conc. $\mathbf{H_2SO_4}$ + crystal of $\mathbf{K_2Cr_2O_7}$—Yellowish-brown coloration.
3. Conc. $\mathbf{HNO_3}$—Red coloration, turning yellow on heating, and turning to purple with $\mathbf{SnCl_2}$.
4. Conc. **HCl,** followed by dilution with water and addition of chlorine water—Red coloration.

To solutions of its salts add—

$\mathbf{Hg(NO_3)_2}$, to a neutral solution—Crimson colour on continued boiling.

**Coniine,** $\mathbf{C_8H_{17}N}$.—Colourless, oily liquid, turning brown on exposure to air; volatile in steam; B.P. 167°; readily soluble in water and organic solvents; *d*-rotatory.

1. Conc. $\mathbf{HNO_3}$—Orange-red coloration.
2. Phenolphthalein—Turned pink in 50% alcoholic solution.
3. After standing for 5 minutes with alcoholic $\mathbf{CS_2}$, the mixture gives a brown or black ppt. with a drop of very dilute $\mathbf{CuSO_4}$.
4. Albumen—Coagulated.

**Nicotine,** $\mathbf{C_{10}H_{14}N_2}$.—Colourless, oily liquid, turning brown on exposure to air; volatile in steam; B.P. 247°; readily soluble in water and organic solvents; *l*-rotatory.

1. Conc. **HCl**—A light violet or brown coloration on warming, changing to orange with conc. $\mathbf{HNO_3}$.
2. Conc. $\mathbf{HNO_3}$—Orange coloration.
3. Phenolphthalein—Pink colour in very dilute alcohol.
4. Albumen—Not coagulated.

5. On warming 1 drop with 2 c.cs. epichlorohydrin gives a red colour.

**Caffeine (Theine), $C_8H_{10}N_4O_2 + H_2O$.**—Colourless needles; M.P. 234°; sparingly soluble in cold water and in alcohol, readily soluble in chloroform; sublimes unchanged.

1. Conc. $H_2SO_4$ + crystal of $K_2Cr_2O_7$—Green coloration.
2. Conc. **NaOH** and boiling—Methylamine evolved.
3. Murexide test—Treat with a crystal $KClO_3$ and a few drops of **HCl,** evaporate to dryness; the red residue turns purple with ammonia.

To aqueous solution add—

1. Iodine in **KI**—A precipitate (after acidification); M.P. 215°.
2. $K_4Fe(CN)_6$ and $HNO_3$ (iron free)—Yields Prussian blue on warming.

**Atropine, $C_{17}H_{23}NO_3$.**—Silky needles or prisms; M.P. 115°; very sparingly soluble in water, fairly soluble in ether or benzene, readily in alcohol or chloroform; optically inactive.

1. Conc. $H_2SO_4$ + crystal of $K_2Cr_2O_7$—Dark brown coloration.
2. Conc. $HNO_3$—Boiled and evaporated to dryness, and residue treated with alcoholic potash; yields violet colour.
3. Bromine in **HBr**—Yellow crystalline precipitate.
4. Baryta water on evaporation to dryness—Odour of hawthorn blossom.

**Cocaine, $C_{17}H_{21}NO_4$.**—Colourless prisms; M.P. 98°; slightly soluble in water, readily in organic solvents; *l*-rotatory.

1. Conc. $H_2SO_4$ + crystal of $K_2Cr_2O_7$—Brownish-green coloration, $SO_2$ evolved.
2. Conc. $H_2SO_4$ and a few drops of alcohol—Characteristic odour of ethyl benzoate.
3. Acids (on heating)—Yields benzoic acid and ecgonine (M.P. 205°).
4. $KMnO_4$ to conc. solution—Violet precipitate of the permanganate.
5. $K_2CrO_4$ in presence of **HCl**—Yellow precipitate.
6. Aqueous iodine on solutions of salts yields—per-iodide, M.P. 161°.

## Carbohydrates

The carbohydrates are crystalline or amorphous solids which char on heating, and emit an odour of burnt sugar. They are non-volatile. Some are soluble in water, *e.g.*, sugars; some are insoluble or sparingly soluble, *e.g.*, cellulose and the starches; lactose is much less soluble than glucose. Some reduce Fehling's solution on warming, *e.g.*, glucose, fructose, lactose. Polysaccharides on hydrolysis with dilute mineral acids yield monosaccharides and in consequence reduce Fehling's solution after neutralisation of the reaction mixture.

*General Test for Carbohydrates.*—To a small portion of the carbohydrate with about 5 c.cs. water, 2—3 drops of a saturated alcoholic solution of $\alpha$-naphthol are added, and 2 c.cs. of conc. sulphuric acid. A violet colour is produced and is discharged by alkalis (*Molisch*).

**Glucose, Grape Sugar or Dextrose, $C_6H_{12}O_6$.**—Glucose is readily soluble in water and crystallises therefrom in granules, containing 1 molecule of water of crystallisation, which melt at 86°. From alcohol the anhydrous

compound, M.P. 146°, separates. It has a sweet taste, but not so sweet as cane sugar. It is dextrorotatory, $[\alpha]_D = + 52{\cdot}5°$ (basis of estimation).

1. Heat a small portion in a dry test tube. The hydrated variety melts, then gives off water vapour, and finally blackens owing to deposition of carbon. Odour of burnt sugar emitted.

2. Treat with conc. sulphuric acid. Pure glucose does not char in the cold; on heating a yellow colour is developed which gradually darkens (*cf.* cane sugar). Ordinary commercial glucose is impure and blackens readily on heating.

Use portions of a 10% aqueous solution of glucose for the following tests :—

3. Add a few drops of caustic soda solution and warm gently. The colour of the solution changes through yellow to brown (*cf.* cane sugar).

4. Add a few drops to 10 c.cs. ammoniacal silver nitrate solution and warm in a bath of hot water. Silver mirror formed.

5. Add copper sulphate solution and then excess caustic soda solution. Solution turns violet, but precipitation of copper hydrate does not take place. On warming, reduction of the cupric compound occurs and red cuprous oxide is precipitated (*Trommer's test*).

6. Add a few drops of Fehling's solution and warm. Cuprous oxide is precipitated (*cf.* cane sugar).

7. Treat with lime water. Glucose, unlike fructose, yields no precipitate.

8. Examine in a polarimeter (p. 48). It is dextrorotatory.

9. Glucose yields an osazone (*cf.* cane sugar).

**Fructose, Fruit Sugar or Lævulose, $C_6H_{12}O_6$.**—Fructose is more soluble in water and in alcohol than glucose. From alcoholic solution it may be obtained in crystals, M.P. 95°, but from aqueous solution it is usually obtained as a syrup. It is lævorotatory, $[\alpha]_D = - 95{\cdot}5°$. With phenylhydrazine it yields the same osazone as glucose (p. 290). In most of its reactions it behaves like glucose from which it may be distinguished by its lævorotation, by its yielding a precipitate with lime water, and by its melting point.

Perform similar tests with fructose as described for glucose.

**Sucrose, Cane Sugar or Saccharose, $C_{12}H_{22}O_{11}$.**—Sucrose is very soluble in water from which it crystallises in large monoclinic prisms. It is sparingly soluble in alcohol. It is dextrorotatory, $[\alpha]_D^{20°} = + 66{\cdot}5°$ (basis of estimation), M.P. about 160°.

1. Heat a few crystals in a tube to melting : on cooling, an amorphous glassy mass of " barley sugar " remains. Heat once more (in an oil bath) to 200° ; " caramel "—a dark brown mass—is formed. On further heating charring takes place.

2. Cover a few crystals with water in a beaker, add an equal volume of conc. sulphuric acid, and stir. Much frothing takes place, sulphur dioxide and carbon dioxide being evolved, and a bulky deposit of carbon left (glucose is slowly charred).

3. Warm a few crystals with conc. nitric acid. Note energetic action (see Preparation 184).

Use a 10% aqueous solution of cane sugar for the following tests :—

4. Treat with caustic soda solution and heat. Not turned brown (*cf.* glucose).

5. Add Fehling's solution and heat. No reduction (*cf.* glucose).

6. Add a little dilute sulphuric acid, boil a short time, and neutralise. Then add Fehling's solution and heat. The mixture of glucose and fructose, known as "invert sugar," brings about reduction to cuprous oxide.

7. Examine in a polarimeter and note dextrorotation. Then heat with a little dilute sulphuric acid, neutralise carefully, and again examine in polarimeter. Note lævorotation. Fructose is more lævorotatory than glucose is dextrorotatory.

**Lactose, Milk Sugar, $C_{12}H_{22}O_{11}$.**—Lactose is much less soluble in water and in alcohol than the other sugars. It is not very sweet. $[\alpha]_D^{20°} = + 52{\cdot}5°$ ; M.P. 205°.

Perform tests for lactose similar to those described under cane sugar. It reduces Fehling's solution on warming, and yields an osazone (distinctions from cane sugar) ; the osazone does not separate very readily from the hot solution (distinction from glucose). It may also be distinguished from glucose by the facts that it is not sweet, it is much less soluble, and it is not so strong a reducing agent.

## Osazones

Mulliken has based a scheme for the identification of pure sugars on the time of formation of their osazones :

Place 0·1 gm. of each of the following sugars, 0·2 gm. of phenylhydrazine hydrochloride, 0·3 gm. of sodium acetate, and 2 c.cs. of water in small test tubes ; cork loosely to prevent evaporation and heat in a boiling water bath. Shake the tubes occasionally without removing from the bath. Note the time required for the separation of precipitates.

| Sugar. | Time. |
|---|---|
| Fructose . . | 2 min. |
| Glucose . . | 4 to 5 min. |
| Sucrose . . | 30 min. (due to slight inversion). |
| Lactose . . | No precipitate in hot solution. |

## Starch

The appearance of different kinds of starch under the microscope is characteristic. Starch is insoluble in cold water, but when heated the granules swell up and burst ; their contents (granulose) dissolve and the cell walls remain in suspension, giving an opalescent solution.

1. Heat a small quantity in a dry tube. Water and combustible gases are evolved and an odour like that of burnt sugar is emitted.

2. Heat a small portion with conc. sulphuric acid. Carbon dioxide and sulphur dioxide are evolved with charring.

3. Mix 1 gm. into a paste with 5 c.cs. cold water and pour into 50 c.cs. of boiling water. Treat portions of the solution as follows :—

(*a*) To a cold portion add iodine solution (iodine dissolved in potassium iodide solution); a deep blue coloration is produced. Boil the solution and note the disappearance of the colour, which reappears, though more feebly, on cooling.

(*b*) To the major portion add 2 c.cs. of dilute sulphuric acid and boil gently under reflux. At intervals of 5 minutes withdraw a portion, cool, and test with iodine solution. The blue coloration due to starch gradually disappears. An intermediate stage (dextrin) occurs when a port wine coloration is obtained with iodine.

## Glucosides

The natural glucosides are complex compounds of the sugars (generally glucose) with organic compounds. On hydrolysis with alkalis, mineral acids, or with ferments they yield a sugar and one or more other organic compounds.

Salicin (from willow bark) on hydrolysis yields glucose and saligenin (*o*-hydroxybenzylalcohol):

$$\underset{\text{salicin}}{C_{13}H_{18}O_7} + H_2O \longrightarrow \underset{\text{glucose}}{C_6H_{12}O_6} + \underset{\text{saligenin}}{C_6H_4(OH)CH_2OH}.$$

Salicin is met with as colourless, glistening, crystalline plates, or as a white powder. It is moderately soluble in water, less soluble in alcohol, and insoluble in ether; M.P. 200°.

1. Treat salicin with conc. sulphuric acid. Deep red colour in the cold.

2. Dissolve salicin in hot water, add a little conc. hydrochloric acid, boil, cool and filter off the saligenin; neutralise filtrate, add Fehling's solution, and warm. Reduction due to glucose.

3. Warm with dilute sulphuric acid and potassium dichromate. Odour of salicylaldehyde similar to meadow sweet.

4. Heat on a porcelain lid. Odour of burnt sugar.

*Amygdalin* (the glucoside of bitter almonds) is a white crystalline compound, soluble in water, readily hydrolysed on heating with dilute sulphuric acid to benzaldehyde, hydrocyanic acid and glucose.

$$C_{20}H_{27}O_{11}N + 2H_2O \longrightarrow C_6H_5CHO + HCN + 2C_6H_{12}O_6.$$

1. Heat amygdalin with dilute sulphuric acid under reflux for a short time. Remove benzaldehyde and hydrocyanic acid by steam distillation. Test for benzaldehyde (phenylhydrazone test) and hydrocyanic acid (Prussian blue test) in distillate, and for glucose (osazone test) in residue.

2. Treat with conc. sulphuric acid. Deep red colour in the cold.

Suzanne V. Cox
Oct. 1939

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Date 10/12, 1939

Name Suzanne Cox

Address

| | | Account Forwarded | | |
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| 1 | Cummings | | 8 | 10 |
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FORM 121 SUNSET-McKEE SALESBOOK CO. — SPOKANE, OAKLAND, SEATTLE

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